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FOR THE GOOD OF THE ORDER

THOMAS D MOORE

The American Urological Association was founded by the late Dr Ramon Guteras in a tavern of Bohemian ownership in New York City in 1902. It was patterned after the French Urological Society, which had been organized 6 years previously. There were 27 original members and by the end of the first year the roster had increased to 89. Although none of the actual founder group is living today, four members survive who were elected to membership in 1902, including 2 Past Presidents, Dr Frederick W Robbins and Dr Louis E Schmidt, both of whom were elevated to the rank of honorary membership in 1949.

Before the American Urological Association convenes again we shall have passed the fiftieth anniversary of its founding, February 22, 1952. Therefore, it seems fitting at this time to pause and take stock of this great organization, with a brief review of past accomplishments together with an assiduous attitude toward future advancement. The Constitution and By-Laws clearly state that the objects of this Association are "To encourage the study, improve the practice and elevate the standards of urology."

It has been my privilege to serve this organization in an official capacity for a total of 14 years, the first 5 of which were as a member of the Executive Committee representing my Section, 7 years as Secretary, and the past 2 years as President-Elect and more recently your presiding officer. Through the years I have been accorded an unusual opportunity to observe the mechanism of the organization. Of particular interest has been the evidence of steady progress in the elevation of urological standards and the increasing degree of prestige maintained by the American Urological Association. From a lowly beginning urology has emerged as one of the true surgical specialties, having gained its proper place in the sun. My official connection with the organization has made it possible for me to become acquainted with a great many of the members and some of the thoughts which will be expressed here today have been prompted not only by specific recommendations received from others but by suggestions picked up casually through informal conversation at various times.

GROWTH OF AMERICAN UROLOGICAL ASSOCIATION

The organization has maintained a steady growth. In all, 2,189 members have been elected and there has been a loss through death and resignation of 833, making a total membership of 1,356 as of this date (fig 1). The elections to membership since the founding of the American Urological Association average 47 per year and the net gain per year has been an average of 26 members.

It would be difficult to determine just how many potential members there are at the present time. I refer to those urologists who possess the qualifications but who have not become affiliated with the organization. The most recent Directory

Presidential address read at annual meeting, American Urological Association, Chicago, Ill., May 23, 1951.

of the American Medical Association lists 2,274 physicians who state that they limit their practice to urology and 622 others declare that they are especially interested in urology but do not limit their practice to this field. Oddly enough, it is found that the total membership of the 8 Sections is 2,272, just 2 less than the number listed in the American Medical Association directory as limiting their work to urology.

The geographical area covered by the active membership includes the United States and its dependencies, Canada, Cuba, Mexico and the Islands adjacent to North America. This great territory has been divided into 8 Sections (fig. 2). There are a total of 1,302 active and senior members in the national organization. On the map the top figures give the number of members of the American Uro-

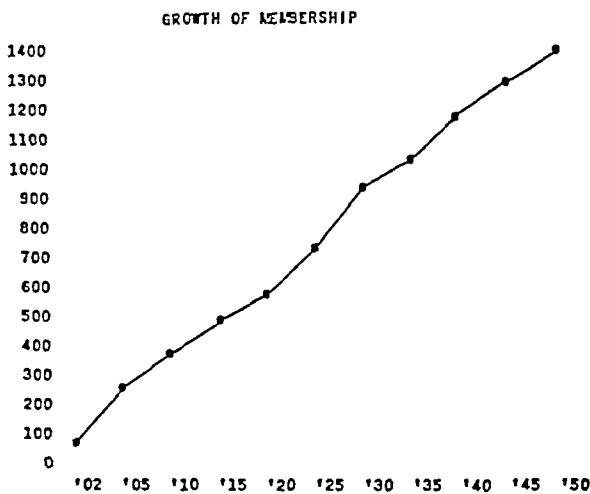


Fig. 1 Growth of membership

logical Association residing in each Section and the percentage of the total membership within the jurisdiction of each Section. Underneath, in parentheses, is the number of members who belong to each Section and the percentage of the members of the Section who are members of the parent organization. The North Central Section has the largest membership, with 21 per cent of the total members of the American Urological Association. From 44 to 72 per cent of the members of the various Sections belong to the national organization, and here again the North Central Section leads with 72 per cent.

Each of these Sections is autonomous as to its requirements for membership and its own governing Constitution and By-Laws, which, however, must be compatible with those of the national organization. It should be emphasized, however, that membership in a Section does not imply membership in the American Urological Association.

AMERICAN UROLOGICAL ASSOCIATION AND THE AMERICAN BOARD OF UROLOGY, INC

To date 1,584 certificates have been issued by the American Board of Urology, Inc. Of this group the Board has been notified of 106 deaths, leaving a total of

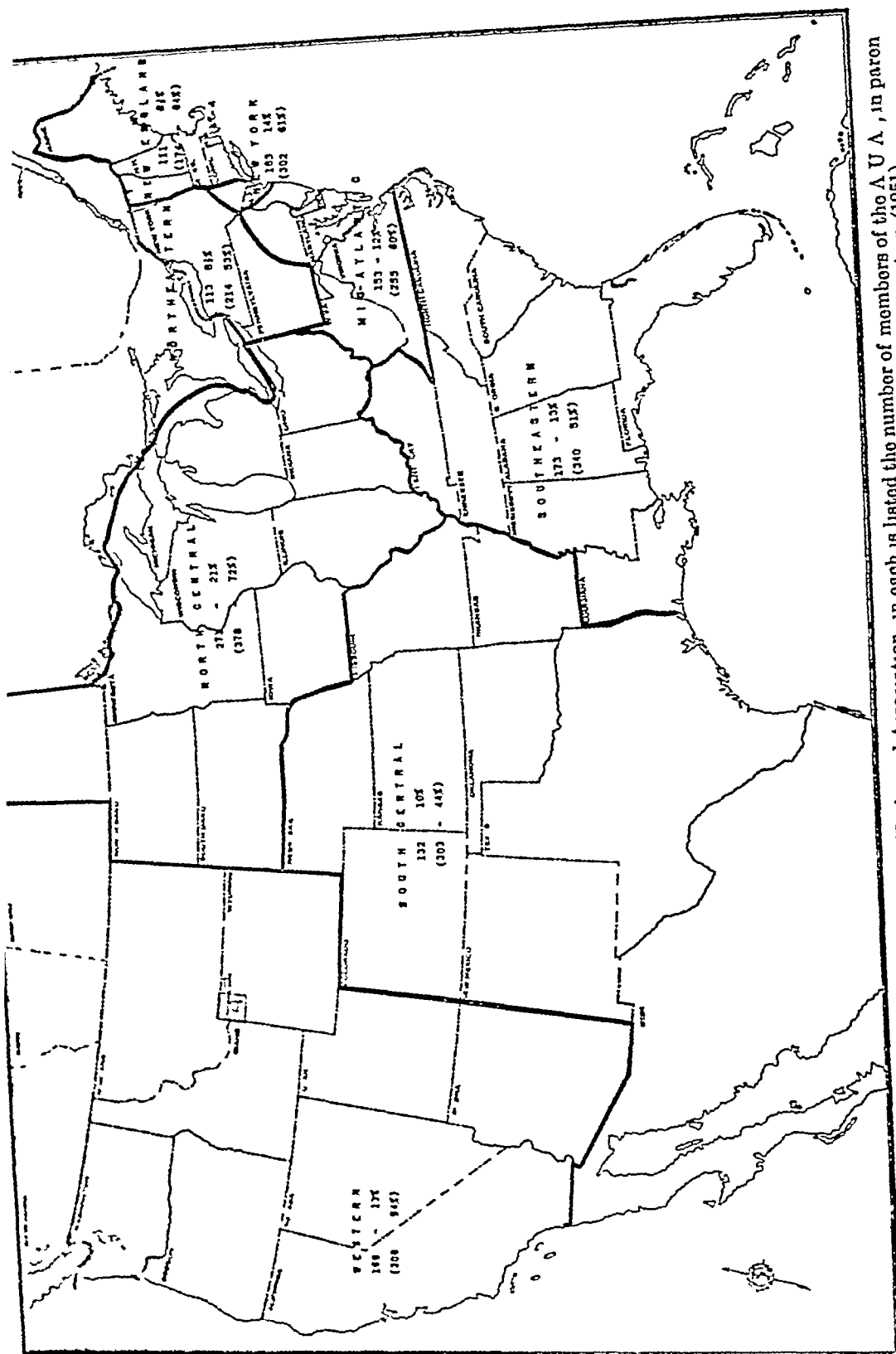


Fig 2 The eight geographic Sections of the American Urological Association, in each is listed the number of members of the A U A , in parentheses is the number of members of the Section with the percentage affiliated with the parent organization (1951)

1,478 active urologists who have been certified by the Board Investigation reveals that of the 1,356 members of the American Urological Association, 933 (69 per cent) have been certified. Of the 1,478 certificatees of the Board, 545 (37 per cent) are not included among the members of the American Urological Association, but 323 out of this group (or 22 per cent) are members of Sections and will no doubt in due time apply for membership in the parent organization.

It appeared worthwhile to determine whether certification by the Board or membership in the American Urological Association was usually attained first. The impression had been gained that many urologists first obtained certification. One possible reason for this is that among the requirements for membership in the American Urological Association are active membership in a Section and endorsement by the Section's Executive Committee, incurring a delay of about 2 years or longer before eligibility for membership in the national organization is attained. An investigation of the 454 members elected to the American Urological Association since 1940 reveals that 378 (or 83 per cent) have been certified. Forty-three (11 per cent) received certification the same year they were admitted to the American Urological Association. Eighty-one (or 22 per cent) were elected to membership in the American Urological Association before attaining certification and 254 (or 67 per cent) were certified by the Board before they became members of the A.U.A., thus confirming the original impression.

The relationship between the Board and the American Urological Association has been the subject of considerable discussion in recent years, especially among applicants for membership. A common inquiry is why should the submission of case reports be required of an applicant who has already been certified by the Board. There have been instances where diplomates of the Board have been denied membership in the American Urological Association and likewise the Board has refused to grant certification to some applicants who had previously been accepted by the American Urological Association. As a member of the Board, I know personally of the searching investigation which is conducted of applicants for certification, including not only the grading of case reports but also written and oral examinations, which test the applicant's knowledge of the basic sciences and all phases of urological practice, with special reference to his diagnostic acumen and surgical ability.

On the other hand, the qualifications of an applicant for membership in the American Urological Association are judged almost entirely by the impression gained by the Membership Committee after a careful review of the case reports he has submitted. It should be emphasized, however, that these records are not judged by only one man but actually by 3 members of the 9 man Membership Committee, which is composed of men fairly distributed geographically about the United States. Because so much emphasis has to be placed on the case reports some applicants for membership in the American Urological Association who have already passed the more searching examination of the Board and who no doubt are well qualified urologists might be denied membership because they are not able to submit acceptable case reports. At first thought this would appear to be a paradoxical situation but after due consideration it would seem that all

competent urologists should certainly be able to qualify in this respect. For instance, of the 42 candidates to be voted upon this afternoon all but 5 have previously been certified by the American Board of Urology. It is quite possible that membership in the American Urological Association may mean more to these men because of the fact that it was attained on an entirely independent basis, rather than automatically because they had been previously certified by the Board. Furthermore, in view of the fact that the majority of applicants for admission to the American Urological Association have already been certified by the Board 2 or more years before, there has been an opportunity for those practicing in their vicinity to formulate an opinion not only of their professional ability but of their ethics. I am sorry to state there have been some instances in which membership in the American Urological Association has been denied a certificatee because of the discovery of unethical practices. For these reasons it may be regarded as a healthy situation to have the requirements of the Board and of the American Urological Association entirely separate and independent of each other.

REQUIREMENTS FOR MEMBERSHIP

There are some medical organizations to which one may not apply for admission but membership is gained only by being proposed. The American Urological Association, however, has been built on broad democratic lines and has always duly considered application for membership from anyone who can meet the requirements. I am convinced that this policy should continue. It has been suggested that the membership numerically should become more restricted or limited but it is believed that this can be accomplished best by continuing to raise the requirements for membership as has been done from time to time in the past. The American Urological Association was organized at a time when urology was branching off from the fields of general medicine and surgery. In 1911 the late Dr. Hugh Cabot in his presidential address stated, "It remains a fact that in the eastern part of the country, at least, serious doubts still exist as to the propriety of giving to those who wish to pursue urology opportunities and hospital accommodations which will enable them to do their work under a satisfactory and profitable environment. It is a curious but noteworthy fact that until the last few months there was not in New England a single large hospital making any separate or distinct provision for the study of urology except in the out-patient department, and no surgeon controlled any beds for the prosecution of this work." In the discussion that followed, some of the leading urologists of that day were of the opinion that surgery of the kidney and of the ureter should be left in the hands of the general surgeon, who was regarded then as better trained to deal with major surgical problems than the urologist. The late Dr. John R. Caulk stated that he took over the Department of Urology of Washington University in 1915 and was granted supervision of all urinary diseases in men, women and children. He felt that this was quite an achievement since there were but very few such departments in America at that time. Even as late as 1930 Dr. Joseph F. McCarthy, in his presidential address, referred to

the varied interests within the speciality There were some who were chiefly concerned with the surgical problems, others were mainly interested in urologic diagnosis, there was a fairly large group devoting much of their time to venereology and small groups whose chief interest was in the urology of children and of women

Urology as a speciality received a great impetus with the evolution of the cystoscope and the discovery of the roentgen ray The speciality has gained tremendously in favor and prestige because of the accuracy of diagnosis and great improvements in surgical technique The urologist is now universally accepted as an established specialist who is accorded an important and definite position among the personnel of the staff of all hospital and teaching institutions For many years those engaged in the speciality were often referred to as doing "G U work" Dr Louis E Schmidt has been given credit for first using the term urology, and in my own section of the country the term "G U" has come to be regarded as denoting "gonorrhea unlimited"

TABLE 1 *Requirements for membership*

YEAR ADDED	
1920	Receipt of doctor's degree at least five years prior to admission
1923	Two of above five years shall have been devoted to urology
1931	Hospital internship of at least one year
	Membership in American Medical Association
	Presentation of triplicate copies of 25 major urological case histories
	Endorsement by two members of American Urological Association and two other physicians
1940	Membership in Section of American Urological Association and endorsement by its Executive Committee
1946	Applicant's training and evidence he submits of his work must cover all phases of urology
1947	Limitation of applicant's practice to 100 per cent urology

Table 1 lists the present basic requirements for membership in the American Urological Association and gives the date each was added Prior to 1947 applicants had been required to limit their practice to at least 75 per cent urology Throughout the years there have been few changes in the basic requirements for membership It was in 1931 that a year of hospital internship was added and there would appear to be good reason for not increasing the training requirements more at that time because facilities for urological training throughout the country were very limited and not until comparatively recent years have a sufficient number of residencies become available to permit formal training on an extensive scale At the present time the Council on Medical Education and Hospitals of the American Medical Association have an approved list of 213 hospitals for urological training, which offer a total of 485 residencies Inasmuch as widespread opportunities are now available for those interested in developing a thorough knowledge of the speciality it would seem reasonable at this time to add to the requirements for membership in the American Urological Association Of course the general economic conditions enter the picture and requirements at

present should not be placed at too high a level Universal military training is in the process of adoption, signifying that every young man must give approximately 2 years of his life to the service of his country and at a time when his education will be seriously interrupted with consequent deferment of his professional training At the same time, we should keep in mind our objective as outlined in the Constitution, "To improve the practice and elevate the standards of urology" Therefore, I should like to offer for your consideration the following suggestions pertaining to the requirements for membership in the American Urological Association There should be a period of training following the 1 year's internship of not less than 3 years in an approved residency, at least 2 of which should be spent in urology and 1 may be served in general surgery In an occasional instance this might work a hardship on certain individuals who in the past might have received excellent training on a preceptorship basis and who are well qualified urologic surgeons but for some reason might be applying late for membership in the organization For this reason, the following might be added This requirement may be abated by action of the Executive Committee

There is one other suggestion which might be made with regard to applications for membership According to the present By-Laws, the applicant must be endorsed by 2 members of the Association and also he gives as references the names of 2 other physicians who are not necessarily members of the Association Actually the 2 letters from non-members have proved to be of little benefit in judging the applicant's qualifications It is suggested that the applicant continue to submit names of 2 members of the American Urological Association who will sponsor his application but that the requirement of 2 other references from individuals who are not necessarily members of the Association be waived Instead of this, the Secretary should direct letters to 2 or more members of the Association who reside in the vicinity of the applicant, soliciting confidential information regarding his professional ethics and personal qualifications Such letters should prove to be of much more value to the Membership Committee

Of interest are the requirements for membership in the various Sections of the Association, 4 of which exact from applicants 100 per cent practice of urology and the other 4 Sections require the practice of 75 to 95 per cent urology All but one of the Sections offer associate memberships It appears advisable that Sections should formulate their own rules regarding membership as the situation varies considerably in different parts of the country However, it would seem reasonable for the American Urological Association to recommend to all of the Sections that associate membership should be reserved for those who are not limiting their work strictly to urology In the future the Sections should admit to active membership only those who meet the requirements for membership in the parent organization

FINANCES

The dues of the American Urological Association were originally \$5 per annum and the initiation fee was \$10 In 1923 both were raised to \$15 In 1930 the initiation fee was again raised to \$25 but the annual dues were not increased Not

until 19 years later, 1949, was there any further change, when dues were raised to \$25 and the initiation fee was made \$50

In an effort to determine how our dues and initiation fees might compare with other groups, letters were directed to 53 medical specialty organizations. Replies were received from all but because of the small size of some of the groups it seemed wise to delete them from consideration. It was evident that 40 of these groups might be considered on a comparative basis with the American Urological Association, with particular reference to size and as far as could be determined on the basis of the scope of their activities. The average number of members for the 40 groups was 1,417. The annual dues of the 40 groups varied from \$10 to \$50 and averaged \$23.50, which compares with our \$25 dues. Seven

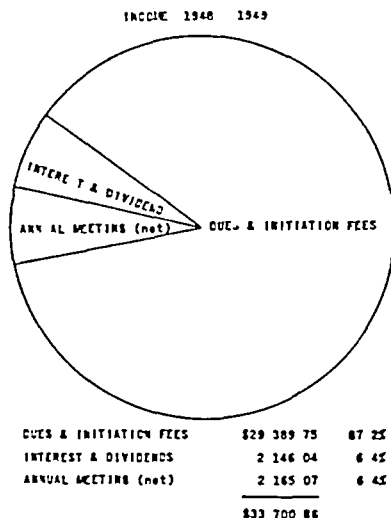


Fig 3 Source of income 1948-1949

of the societies had initiation fees of \$100 and the average for the 40 groups was \$40, as compared to our \$50 initiation fee. It might be mentioned that quite a number of these groups stated that they planned to raise their dues and initiation fees this year because of the increased costs of operating.

Figures 3, 4 and 5 reveal the sources of income of the American Urological Association during the past 3 years, with the percentage derived from each. The annual dues and initiation fees are constant sources of income, which have not varied much from year to year. Other potential sources of income are those from the investment of accumulated funds, the net income, if any, from the annual meetings, and receipts, if any, from the publication of the *Journal of Urology*. You will notice that income was derived from both the annual meeting and the *Journal of Urology* in 2 of the 3 years studied, indicating that they are not sources of income which can be depended upon because in some years a deficit will be sustained whereas in others a surplus will accrue. In the past year a nice increase in income was received from both the annual meeting and from the *Journal of Urology*. As for the annual meeting it is difficult to understand how the

Chairman of the Arrangements Committee, Dr William P Herbst, was able to do such a fine job at Washington and turn over this substantial surplus. Although in times past often there has been a small surplus from annual meetings it has never approached the figure it did last year and it should not be expected that

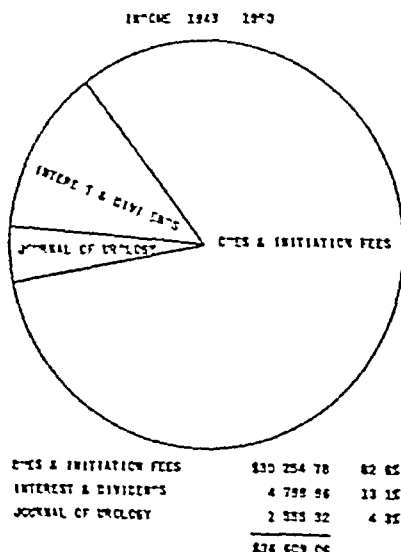


Fig 4 Source of income 1949-1950

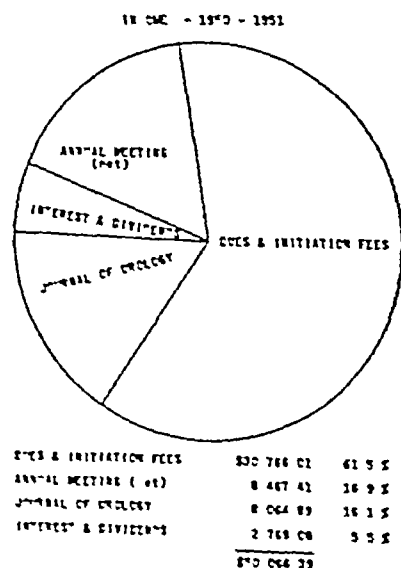


Fig 5 Source of income 1950-1951

such will occur again soon. Actually the surpluses which have resulted from a few meetings in the past have been just about cancelled by deficits at other meetings.

Perhaps you will be more interested in the disbursements, the nature of which is revealed in figures 6, 7 and 8, covering the last 3 fiscal years. It will be noted that the bulk of income is returned to the membership in the form of subscrip-

tions to the *Journal of Urology*, together with the expense of the Editorial Office, which average about 35 per cent of the total over the 3-year period. There is always a potential source of income from the *Journal of Urology*, although occasionally a deficit occurs. During the past 3 years a total of \$9,620.21 has been received from the publishers of the Journal, representing a rebate to which the Association is entitled under our contract with the publisher, depending upon the number of subscriptions sold and the number of pages utilized in the production of our official organ.

In the survey of the medical specialty groups referred to above, it was found that 25 publish medical journals, subscription to which is included in the payment of annual dues. It was interesting to note that the average amount allotted

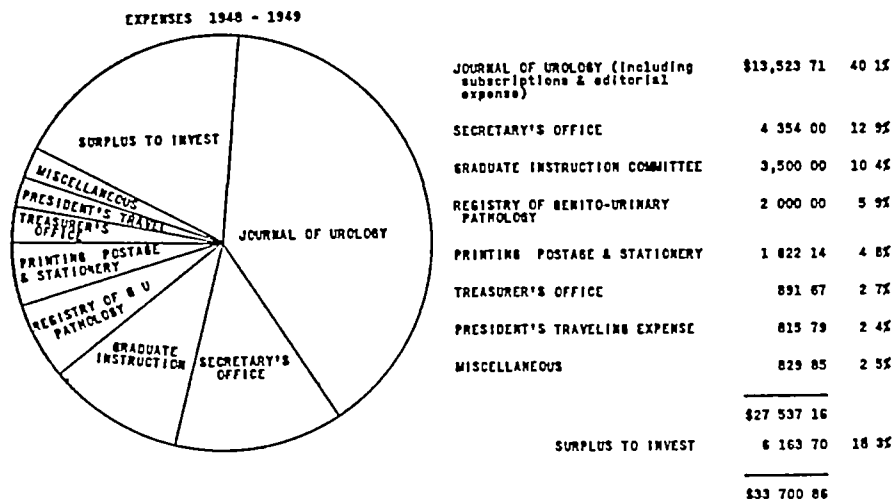


Fig 6 Disbursements 1948-1949

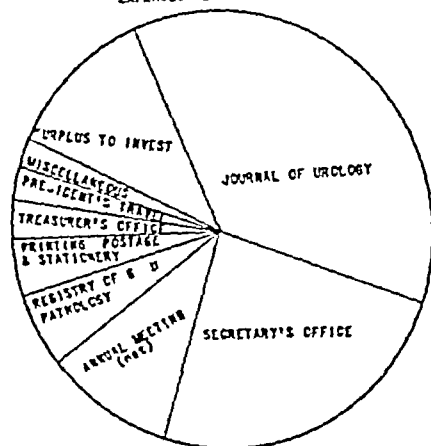
for publication of the various journals by the 25 groups was 39 per cent of their dues. It would therefore appear that the cost of the *Journal of Urology* is on a par with that of other national medical organizations.

The Association should be forever grateful to the late Dr. Hugh H. Young for the active part he played for so many years as Editor-in-Chief of the Journal, which holds a very high rank among scientific publications. The present Editor, Dr. J. A. Campbell Colston, and the Associate Editor, Dr. Hugh J. Jewett, have maintained an exceedingly high standard and it is generally conceded that there is no better urological publication in the entire world.

The next largest expense has been incurred by operation of the Secretary's office, which has increased from 13 per cent to about 25 per cent during the past 3 years. This outlay is for a most important purpose as through this office the membership is kept fully informed of the affairs of the Association. Here all the archives of the Association are safely kept, and here the general business of the organization is conducted, including all correspondence regarding applications for membership, notification to all committeemen, formulation of the official programs and from time to time the issuance of News Letters and regularly

revised editions of the Roster and Constitution and By-Laws Two years ago a separate office was established in Atlantic City for conducting the entire work of the Secretary's office Prior to that time the professional offices of the official secretary had been utilized for these activities It became apparent, however, that this arrangement involved an imposition on the professional office space of

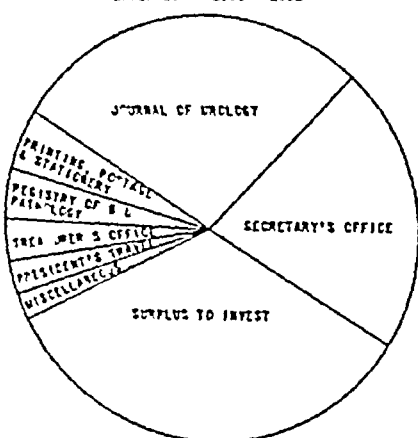
EXPENSES 1949 - 1950



JOURNAL OF UROLOGY (including subscriptions & editorial expense)	\$13,264 80	36 2%
SECRETARY'S OFFICE	9 060 23	24 8%
ANNUAL MEETING (net)	3 602 01	9 8%
REGISTRY OF GENITO-URINARY PATHOLOGY	2 000 00	5 5%
PRINTING POSTAGE & STATIONERY	1,586 97	4 3%
TREASURER'S OFFICE	1,054 15	2 9%
PRESIDENT'S TRAVELING EXPENSE	1 000 00	2 7%
MISCELLANEOUS	700 84	1 9%
	\$32 269 00	
SURPLUS TO INVEST	4 340 06	11 9%
	\$36 609 06	

Fig 7 Disbursements 1949-1950

EXPENSES - 1950 - 1951



JOURNAL OF UROLOGY (including subscriptions & editorial expense)	\$14 022 29	28 0 %
SECRETARY'S OFFICE	11 223 27	22 4 %
PRINTING POSTAGE & STATIONERY	2 078 11	4 2 %
REGISTRY OF GENITO-URINARY PATHOLOGY	2,000 00	4 0 %
TREASURER'S OFFICE	1 375 27	2 8 %
PRESIDENT'S TRAVELING EXPENSE	1 265 87	2 5 %
MISCELLANEOUS	1 005 28	2 0 %
	\$32,973 09	
SURPLUS TO INVEST	17 093 30	34 1 %
	\$50 066 39	

Fig 8 Disbursements 1950-1951

the Secretary and the Executive Committee wisely authorized the establishment of a separate office in 1949 The high degree of efficiency with which this office has been conducted under the guidance of the Secretary, Dr Charles H deT Shivers, and his capable secretarial assistant, Miss Dorothy Nyquist, is well known The expense of maintaining such an office, however, has necessarily increased appreciably, approximately 25 per cent of the total income can be reasonably allotted for this purpose This could be subject to a definite increase at some future time, however, should the Secretary's Office be moved to some

other location because the rental rate on the space now occupied is only \$1 00 per square foot per annum, whereas in most metropolitan areas such office space rents for \$3 00 to \$5 00 per square foot

In the last 3 years after all expenses were paid the Treasurer has had on hand surplus funds for investment varying from \$4,340 06 to \$17,093 30 (or 11 9 per cent to 34 1 per cent of the total income) On the surface this would appear to indicate a very favorable financial condition of the American Urological Association On the other hand, it should be kept in mind that the Association's income can be seriously affected by prevailing economic conditions For example, during World War II 24 per cent of the members of the American Urological Association served with the Armed Forces and were granted remission of dues during their period of service In the event of another major conflict, which at present does not appear beyond the realm of possibility, a large number of members would serve again in the Armed Forces and the Association thus would be confronted with a great loss of income At the same time, the fixed overhead expenses would continue, necessitating the possible use of reserve funds Also, it should be pointed out that there are a large number of active members, approximately 25 per cent, who are eligible for transfer to senior membership as provided by the By-Laws, with waiver of dues If this group were prompted to exercise this right under the stringency of a period of declining prosperity and high taxation an additional very serious loss of income would be incurred

It is generally known that the income provided by the yield on invested funds has become alarmingly low with the advent of inflation and cheaper money Particularly has this been true of investments in bonds which formerly yielded around 5 per cent and comprised a real source of income for the Association This has been offset to some extent by investment in some high grade common stocks which provide a definitely higher yield This has been accomplished under the guidance of our financial adviser, the New England Trust Company, and is in line with the policy adopted by trusts and educational institutions, such as some of the leading universities, many of which have found it difficult to meet their obligations from income formerly derived from their invested endowment funds

At this time a further increase in dues, or in the initiation fee, does not appear necessary but a careful watch should be maintained on the ratio of income to expenses If possible, a substantial balance should be kept in the Treasury in the event that circumstances might seriously curtail income

For several years past the annual report of the Treasurer has appeared increasingly favorable and the assets of the organization have reached an all time peak It should be remembered, however, that the dollar has been greatly devalued and at the present time is actually worth only about 55 cents in purchasing power Regarded in this light the actual number of 100 cent dollars in the Treasury is less than the number we were able to report 10 years ago Inflation is our common enemy and will remain so until the era of deficit spending has ceased Disbursement of these cheaper dollars by action of the Executive Committee should be on a guarded basis, with particular reference to large

appropriations for any new ventures To the altruistic-minded it might be mentioned also that through the years these funds have been garnered from the members of the American Urological Association who very definitely rate priority in any benefits to be derived from their spending

The Association has been especially fortunate in having had the benefit of such astute custodians of its pursestrings in recent years as Dr James B Cross, Dr Herbert H Howard, and the present Treasurer, Dr George C Prather To them is due a great deal of gratitude for the healthy financial status of the Association at this time

RESEARCH PROGRAM

The American Urological Association has always encouraged in every way possible research designed to carry forward the frontier of urologic knowledge As evidence of this are the contributions made through the years to the Registry of Genito-Urinary Pathology, the awarding of prizes in the Scientific Exhibit, the Prize Essay Competition, and more recently the annual award for meritorious work in the human male reproductive tract At the meeting in Washington, D C in 1950 a Committee on Research Finance, of which Dr Charles C Higgins is Chairman, was appointed for the purpose of exploring the possibilities of securing additional sources of income for research

In order to obtain information regarding the possibilities, the 40 medical organizations referred to above were questioned regarding financial help they were receiving from outside sources Twenty-three of the organizations have not in the past nor are they at the present time receiving revenue other than from annual dues Nine of the organizations have received or are now receiving money from philanthropic sources for research One group receives \$1,500 per year from an endowment fund, another \$5,000 yearly for research fellowships, a third had received bequests in the amount of \$10,000 and a fourth society has \$90,500 which has been received from research foundations for special projects Four of the organizations have received contributions from commercial and industrial manufacturing concerns, of as much as \$15,000 per year One group mentions a grant of \$40,000 from the U S Public Health Service, but of course this was for a specific research project

Eight of the organizations encourage outright gifts from members and also receive gifts secured from donors through the efforts of individual members of the society In one group, members had subscribed in amounts varying from \$5 to \$50 to build up a capital fund In another instance, the revenue from royalties on instruments was allotted to a society One group mentioned that contributions from deceased members had amounted to \$30,000

Although the By-Laws of the American Urological Association provide that one of the sources of income shall be through voluntary contributions it is interesting to note that no such contribution has yet been received by the organization Possibly this may be explained by the fact that the Association as governed by the Federal laws of Internal Revenue cannot receive such funds on a tax-exempt basis, nor can the donor deduct such funds in computing his income

tax Recently legal advice was sought for the purpose of finding a solution for this problem, as a result of which a plausible plan was evolved Mr Charles P Cobb, a tax attorney of Memphis, Tennessee suggested that a separate organization be incorporated under some such name as "The American Urological Research Foundation, Inc" which would meet all of the requirements of the Internal Revenue Code, specifically exempting the fund from taxation and also making possible the deduction of contributions by individuals or other interests in computing their income tax If the "American Urological Research Foundation" qualified as a corporation, whose income would not be subject to federal taxation, it would also qualify as a non-profit corporation, contributions to which would be deductible by individuals in computing their own personal income taxes Private corporations are allowed similar deductions for contributions to such organizations within certain limits

It is quite possible that there are a number of members who might favorably consider a contribution to such a fund in planning their estates or as voluntary contributions which would be deductible from the currently high income tax Other sources of revenue for research purposes might be commercial interests which have greatly prospered from the support of urologists, or grateful patients who might express a desire to make a substantial contribution to urological research An example of this occurred about 4 years ago when a very wealthy patient who had apparently completely recovered from a carcinoma of the prostate expressed a desire to show his gratitude to his surgeon, the late Dr E Granville Crabtree, by donating up to \$15,000,000 for urological research It was Doctor Crabtree's idea that this fund should be placed under the supervision of the American Urological Association but his untimely death unfortunately caused a cancellation of the plan and the funds were directed into other channels

Through the influence of the Committee on Research Finance the obtaining of grants from philanthropic sources might be facilitated for the benefit of the individual research worker It is suggested that this committee be maintained as a permanent arrangement and that every effort be made to accumulate a fund which would be earmarked for use only for research purposes under the guidance and responsibility of this committee

PROGRAM OF GRADUATE INSTRUCTION

The program of postgraduate seminars was inaugurated in 1948 when a committee on Graduate Instruction was appointed with Dr William F Braasch as Chairman The work of this committee has stimulated tremendous interest in graduate instruction and 13 seminars have been conducted to date in 7 Sections of the Association The Western Section has sponsored 4 such courses, the North Central, South Central and Southeastern 2 each, and there has been 1 each in the Mid-Atlantic, New York and Northeastern Sections The Northeastern and Western Sections have already announced plans for additional courses this fall There has been a total registration at the 13 seminars of 1,775 and the attendance has varied from 64 to 200 They have definitely provided a

means for the urologist to improve his knowledge of various aspects of the practice of the specialty, along with a review of the sciences basic to urology. Of equal importance is the opportunity provided by these seminars for younger urologists to take intensive instruction designed to better qualify them for passing the Board examinations. The seminars in the main have been self-sustaining and in some cases a substantial surplus has accrued after all expenses have been met.

Certainly it should be the policy of the American Urological Association to continue to sponsor this plan of graduate instruction and to lend it an increasing degree of financial support if necessary.

ESTABLISHMENT OF LIBRARY OF FILMS

For some years the Motion Picture Program, as conducted under the guidance of the Committee on Visual Education at the annual meetings, has proved to be a very important and most instructive project. It is unfortunate that the best of these films which have been exhibited through the years have not been accumulated in a library sponsored by the Association. It is not too late to establish such a collection by having one or more copies made of films which are recommended by the Committee on Visual Education, and at the expense of the national organization. A custodian for the library could be appointed and the films could be made available without expense to urological groups, medical schools, hospital staff meetings and others interested in their presentation for educational purposes. Although large libraries of films on various topics have been accumulated by the American College of Surgeons and by the American Medical Association, such a library purely urological in nature, sponsored by the American Urological Association, would no doubt have a greater appeal to the average urologist and would go a long way toward elevating the standard of urological practice.

ATTENDANCE AT ANNUAL MEETING

The ever increasing attendance at the annual meeting of the American Urological Association has been a source of encouragement and satisfaction. At the same time it has brought about some real problems. The meeting at Cincinnati in 1946 was the first one where attendance approached 1,000. Since then there have been 2 meetings, at Boston in 1948 and Washington in 1950, at which the registration was approximately 1,500 and the attendance at this meeting compares favorably with these figures. While this is a most encouraging sign, the necessity of arranging a meeting for a group of this size greatly taxes the ingenuity of a local group. It has become increasingly difficult to find a hotel with facilities adequate to accommodate our organization and I refer especially to an assembly room and banquet hall of sufficient size to take care of the entire group. It is very evident that it may be necessary to limit social functions, or as an alternative to schedule the meetings in an auditorium, permitting the members to arrange hotel accommodations wherever they wish, and thus lose the intimacy, comradery and convenience of having the meeting housed entirely

in one hostelry One possible solution of the problem would be to limit attendance at the social functions to the actual members of the organization and their personally invited guests It is suggested that Arrangements Committees have the prerogative of doing this in the future if there is any question about adequate facilities for the social functions It is to be hoped that it will not be necessary to limit attendance at the Scientific Sessions and that a meeting room of sufficient size to accommodate all who desire to attend the annual conclave will always be available Many of the younger urologists and other physicians who are not members derive a great deal of benefit from the Scientific Sessions and undoubtedly many are thereby inspired to improve the character of their work, as well as to apply for membership as soon as they can meet the requirements

NOMINATING COMMITTEE

Every effort is made to see that the Sections receive adequate representation in the American Urological Association Each Section of course has an elected representative serving on the Executive Committee and on the Editorial Committee, and also in the appointment of committees a special effort is made to see that each of the 8 geographic Sections receives fair representation This policy is also followed in arranging the Scientific Program, when an attempt is made to select papers from each Section and to further equalize the distribution in the selection of those to discuss papers By having the Sections share in this way in the affairs of the American Urological Association it makes the organization democratic in the true Jeffersonian sense of the word

At the present time the Nominating Committee of the American Urological Association is composed of the 3 most recent Past Presidents, a member representing the Executive Committee, and the fifth member is elected from the floor at the annual business meeting I would like at this time to propose that we further carry out the policy of having the 8 Sections assist in governing the American Urological Association by a revision of the By-Laws to provide the following plan of choosing the personnel of the Nominating Committee Each of the 8 Sections shall elect a representative to serve on the Nominating Committee, and in order to make it an uneven number and to avoid a possible tie, the most recent Past President shall serve on the committee as its Chairman In this way the Sections will fully realize that they are having equal voice in the selection of officers

SUMMARY OF RECOMMENDATIONS

In summarizing, the following recommendations would seem appropriate

- 1) That the requirements for membership in the Association be revised
- a) To include a period of training following the internship of not less than 3 years in an approved residency, at least 2 years of which should be spent in urology and 1 of which may be served in general surgery
- b) The deletion of the requirements that applicants for membership include as references 2 physicians, not necessarily members of the Association Instead, in addition to 2 letters from members of the American Urological Association

listed as sponsors by the applicant, the Secretary will obtain 2 or more letters from other members of the Association who practice in the vicinity of the applicant, to further check on his professional, ethical and personal qualifications

2) All Sections should be encouraged to have a classification of associate membership and in the future to elect to active membership only those urologists who meet the requirements for membership in the national organization

3) That serious consideration be given the establishment of an organization within the American Urological Association, such as The American Urological Research Foundation, Inc, which would be designed to receive contributions for the promotion of urological research The advantages of this arrangement would be two-fold, in that such funds would be exempt from federal taxation and contributions to the Foundation would be deductible by individuals in preparing their personal income tax returns This plan would enable the Committee on Research Finance to exert a greater effort to obtain funds for furthering urological research

4) That a library of urological motion picture films be established

5) That attendance at the social functions at the annual meetings of the American Urological Association be limited to members and their personally invited guests, if in the discretion of the Local Arrangements Committee this is advisable because of limited facilities

6) That the plan of determining the personnel of the Nominating Committee of the American Urological Association should be revised to include a representative selected by each of the 8 Sections, and the Chairman shall be the most recent Past President of the Association, constituting a committee of 9 instead of 5 members

CONCLUSION

In conclusion, I should like to express to the new members a warm welcome to the Association and to urge you to attend regularly the meetings, to give your fellow urologists the benefit of any new ideas or unusual experiences through the preparation of papers, to feel free to participate in the discussion of papers when you have something worthwhile to contribute, and to engage in research whenever possible Your equipment, both mental and physical, is superior to that of your predecessors You have had many advantages in training which were not available to the older members There is still much to be done in the way of research as there are a great many problems in urology which yet remain to be solved From you we are seeking the answers

I should like to express my deep appreciation to the other officers of the Association, to the members of the Executive Committee, and to the Chairmen of the various committees with whom I have collaborated during the past several years, for the splendid cooperation and encouragement which they have given at all times

To all members, I wish to express my sincere gratitude for the privilege and honor of serving in this high office of the largest and greatest of all urological organizations

On the program of the meeting this year there are at least 3 of the same subjects that appeared on the program of the first annual meeting held at Saratoga Springs, New York, June 13, 1902 1) Indications for and technique of nephropexy, 2) treatment of tuberculosis, and 3) operations on the prostate gland It might be stated that our goals and interests have not changed a great deal in the past 50 years and it would appear just as fitting today to close by quoting the last paragraph of the address of the first President of the American Urological Association, Dr Ramon Guiteras "Let us hope that this Association will remain the centre of the growth and development of American Urology, that within its membership will always be found the exponents of conscientious work in the advancement of this branch of medical science, and that it may grow in influence and prosperity from year to year "

899 Madison Ave , Memphis 3, Tenn

CERTAIN CONCEPTS IN HUMAN MALE FERTILITY

JOHN MACLEOD

Department of Anatomy, Cornell University Medical College, New York, N. Y.

During the past 30 years enormous strides have been made in our knowledge of the mechanisms involved in the physiology of human male reproduction. On my entry into the field some 12 years ago, my primary interest lay in the metabolism of the spermatozoa themselves and in the enzymatic processes responsible for the initiation and the maintenance of motility. Though my interest still lies in this fundamental approach it soon became evident to me, as it had to many others, that we actually knew little of the kinetics of human spermatogenesis, of the physiology of ejaculation, of the role of the accessory glands in the delivery of the ejaculate and, what is perhaps most important, what constitutes male infertility. There is no time now to review in any detail the slow but steady accretion of careful, methodical research which only in the past few years has given us a clearer perspective on what must be considered a major problem in medicine today, namely that of male infertility. It is my feeling that the urologists, considered as a profession, have shied away from this subject in their practice of medicine. They do so not because they deny that any such problem exists but because they feel that little can be done by them to alleviate it. They say, "all right, we decide on the basis of a semen examination that a man's fertility is low—is there any sound therapy we can use which will raise his fertility potential?" Those of us who are concerned with academic research must reply that we can offer little. There are even those who say that, assuming a man to be potent, a semen examination means nothing unless it shows a complete absence of spermatozoa. To put this conception another way, it is often said that as long as the seminal fluid contains active spermatozoa, a detailed semen examination will add nothing to our knowledge of the individual's fertility. I hope to show that this somewhat fatalistic attitude is not justified and to define more precisely our concept of human male fertility. Further, I hope to leave you with the feeling that, more than ever, a careful

The author is deeply indebted to Cornelius Vanderbilt Whitney for the financial aid necessary for the continuation of this research.

Read at annual meeting, American Urological Association, Chicago, Ill., May 21, 1951.
Note by editor: Dr. MacLeod was the recipient of the fifth annual award by the American Urological Association for research in the human male reproductive tract. The following citation was read by Dr. Reed M. Nesbit, chairman of the awards committee:

"Six years ago our organization established an award for recognition of individuals contributing importantly to our knowledge of the reproductive process in the male. The award has been made not so much with the idea of bestowing an honor upon the recipient, for his accomplishments already have brought him acclaim, not yet for the purpose of stimulating research for the scientific attitude is not a commodity that can be purchased. It has been made rather in the self interest of bringing to urologists in America outstanding contributions in this field so that we may be better informed, and perhaps better stimulated to investigate deeper into the unanswered mysteries of human reproduction."

This year Dr. John MacLeod, Professor of Anatomy at Cornell University Medical College, has been invited to come here in order to tell us some of the investigations which have contributed so much to our present knowledge of the physiology of reproduction, particularly in the study of human semen."

semen examination is necessary in every case of infertile marriage and that it is the job of the urologists to do it

If I may return for a moment to the question of what can be done to help the "infertile" male, the answer depends in part on our standards for male fertility and what, in terms of semen quality, constitutes male infertility. As most of you know this is still a matter of considerable debate. For example, a sperm count level below 60 million/cc is considered by many to constitute subfertility and it is below such a level that therapy has been considered as necessary in such individuals. When therapy proves of no avail in these cases, as it most often does, the tendency has been for us to despair and search around for another approach. Could it not be that our standards for male fertility are entirely too high and that the range of normal male fertility is much wider than we ever thought? Assuming this to be true, we could explain why therapy seems to fail so often in cases of supposed male infertility. We have tested these possibilities in a statistical analysis of semen quality in the "normal" fertile male and in cases of infertile marriage.^{1 2 3 4} Our criterion for the fertile male is the man who has sired children in a legitimate union and or whose wife was pregnant at the time the semen examination is made. In the vast majority of such cases, these individuals have never felt the necessity of consulting a physician or a clinic for an infertility problem so that there is a population we never see for study. The "infertile" male by our criteria is not necessarily infertile. But he is the individual who consults us because his marriage is a sterile one after one or more years of attempts at conception. It is our job to determine if he is at fault, but in doing so, we are basing our prognosis on semen standards which are based on a study of these very individuals. Why is this so? It is because these are the only men whose semen we *have been able to study*. We do not, or we did not, know if the faults we found in the semen of these men would not be found in equal degree in men of "normal" fertility. The analysis I shall speak of briefly at this point is based on a comparison of semen quality of 1000 men in fertile marriage and in 1000 men in "infertile" marriage. From these data, I believe we are now in a strong position to define standards for male fertility in a more rational way.

We have divided semen quality into four categories, namely, ejaculate volume, sperm count, sperm motile activity and sperm morphology and compared each category in one group with that of the other. Several new conclusions on male fertility are inescapable.

We can neglect, for the moment, ejaculate volume as an important factor though our analysis does show that very high volumes are usually associated with the most infertile men. It is when we compare the sperm count levels in the fertile and infertile groups that certain striking differences are apparent.² It is at the "under 20 million/cc" count level that we see the critical contrast. Only 5 per cent of the fertile men are found in this classification compared to

¹ MacLeod, J. J. *Fert and Steril* 1: 347, 1950.

² MacLeod, J. and Gold, R. Z. *J Urol*, 66: 436, 1951.

³ MacLeod, J. and Gold, R. Z. *J Fert and Steril*, 2: 187, 1951.

⁴ MacLeod, J. and Gold, R. Z. *J Fert and Steril*. In press.

17 per cent of the "infertile" group. In fact, if we take the rather hazy standards which have been used in the past few years, 29 per cent of our fertile group are "subfertile." The 20 million/cc level looms more critically if we analyse the data in another way. If we now combine the fertile and infertile groups (making 2000 cases in all) and classify them according to sperm count/cc in groups of 20 million (1-19, 20-39 etc.) we find, for example, that 211 men from both groups had sperm counts under 20 million/cc and 248 were between 20-39 million/cc. If count/cc were *not* a discriminating factor in fertility one would expect the number of cases falling in each count classification to be evenly divided as to fertility and infertility. This is not the case as is shown by examination of the proportion contributed by the fertile group to each count level. Thus, the fertile group contributed only 22 per cent instead of 50 per cent to the 211 cases under 20 million/cc, a highly significant difference. At the 20-39 million/cc level this proportion jumps dramatically to 47 per cent, not significantly less than the theoretical contribution of 50 per cent. We feel reasonably certain, therefore, that so far as sperm count is concerned at least, the normal standards should be lowered considerably and that the count level of 20-30 million/cc should be considered as the lower level of normal. A further point of importance borne out by this analysis is that there is *not* a proportional rise in fertility potential with rising sperm count above the 20 million/cc level.

A somewhat different story emerges when we analyze the two groups in terms of motile activity³ and sperm morphology.⁴ The fertility potential of the individual rises as the percentage of active cells increases and as the quality of their motile activity improves. There is quite definitely a proportional rise in fertility as these qualities improve. We therefore must take the position that motile activity is more important than sperm count provided the latter is at a certain minimal level.

Similarly, as the percentage of morphologically normal cells increases we find an increasing fertility potential. We are not prepared at this time to discuss the relative importance of morphology as compared to motility. What we wish to emphasize is that the motile activity of the spermatozoa has a distinctly closer relationship to male fertility than does the sperm count. Secondly, we would suggest that therapeutic attempts to raise a sperm count of 20 million to one of 60 or 70 million are probably futile and quite unnecessary if in the semen of that individual the motile activity and the morphology of his cells are good.

A second concept in human male fertility which requires clarification and emphasis and which has a close relationship to what we already have said is the constancy in health of the fundamental pattern of spermatogenesis laid down in the individual. In recent years, and particularly during the analytical study of male fertility we have undertaken, I have been deeply impressed with this fact. It might almost be said that the pattern of spermatogenesis in any given individual in health is as distinctive as his fingerprints, a thought suggested by Moench⁵ many years ago. More particularly, the germinal epithelium in a

³ Moench, G. L. and Holt, H. *Am. J. Obst. and Gynec.*, 22, 193, 1931.

given normal individual produces mature spermatozoa at a constant rate. They appear in an ejaculate which varies little in volume provided the intervals between ejaculation are fairly constant and their number in these ejaculates do not vary much in normal circumstances. This is the quantitative productivity of the germinal epithelium. What of the quality of spermatozoa delivered? In this respect there is a close analogy between the bone marrow and the germinal epithelium. The bone marrow in health delivers red cells and white cells in a certain constant ratio which varies in different individuals but is constant for the individual. The white cells in certain individuals may have characteristics which distinguish them from the white cells of others, but again these characteristics are born of a fundamental pattern laid down in that individual. Similarly, the germinal epithelium of each of us delivers to the ejaculate spermatozoa of varied morphologic types, the ratio of one type to the other being constant from one ejaculate to the next irrespective of the total number of cells delivered and provided the individual is not subjected to stress. We have followed this pattern in many medical students and patients over a period of years at regular intervals. I have been impressed with this qualitative response particularly since we attempt to be as objective as possible in these morphologic examinations. We employ a code system which does not permit the observer to know from whom the spermatozoa under examination originated.

Your attention is drawn to the concept because it provides us with a valuable research tool. We must have wider knowledge of the germinal epithelium and of the kinetics of spermatogenesis. Before we can properly assay the effect of therapy we must have sharp end-points upon which we can rely. We believe we have found such end-points so far as the ejaculate is concerned or, at least, we have sharpened the end-points which existed until recently. But we must eventually be in a position to visualize more clearly the changes in the germinal epithelium which are reflected in rises or falls of the sperm count in the ejaculate. The testicular biopsy is most valuable in giving us a clear picture of the germinal epithelium at the time the biopsy is taken. In the hands of experts a reading of the biopsy specimen does not only give us the state of spermatogenesis, but a few (all too few) competent men can predict from such a reading about how many spermatozoa should be found in the ejaculate and also the morphologic characteristics of these cells. But in spite of the prognostic skill of these observers, it is my strong impression that standards for what constitutes normal germinal epithelium are not yet available to us. The reason for this gap in our knowledge is that virtually all testicular biopsies are done on men who already have abnormalities in the ejaculate. Nevertheless, we can derive a considerable amount of information on the functioning of the germinal epithelium from changes in the quality of the ejaculate which are due to well-defined causes. I am leading now to the third and last concept of which I would like to speak today.

Only a relatively small fraction of male infertility can be ascribed to absolute sterility. The causes of absolute sterility in most cases are well known. They are 1) failure of descent of the testes, 2) failure of development of the germinal

epithelium in otherwise normal testes (this can be due to a variety of causes), 3) mumps orchitis some time before or after puberty, 4) atrophy of the germinal epithelium due to damage inflicted by harmful radiations, particularly x-ray, 5) atrophy of the testes due to trauma during hernia repairs, 6) congenital absence of the epididymis or the ductus deferens or both and 7) bilateral occlusion of the ductus deferens as a result of inflammatory processes, usually gonorrhea. There are other causes but I believe I have enumerated the principal background of absolute male sterility.

The major portion of male infertility (probably about 95 per cent) is to be found in deficiencies in the male reproductive tract which give rise to oligospermia and it is this dyscrasia which has proved least responsive to therapy. We already have defined what we consider "oligospermia." What is the etiology of this condition? First, I should say that none of us can be certain that the actual site of the deficiency is in the germinal epithelium though that is the popular supposition. If we assume for the moment that it is, then is it because a pattern of deficient spermatogenesis is laid down in the embryo when the primordial germ layers are formed or does some environmental factor impose injury when the germinal epithelium becomes fully organized after puberty? We can state with reasonable certainty that, after analyzing the case histories and physiques of thousands of these infertility cases, we can find no common factor or factors which would suggest a reason for oligospermia. Overt signs of endocrine deficiencies are lacking and nutritional factors, as we know them now, do not make themselves obvious. But in the past year we have gathered evidence which shows quite definitely what we had suspected before, namely, that the germinal epithelium is extraordinarily sensitive to changes in its environment.

In my laboratory, during the years, we have endeavored to check the fertility of every male student entering the medical school. We had two objectives in mind when this study began. The first was that we wished to gather data on the so called "normal" individual. The second objective was more far-reaching inasmuch as we hoped to establish controls so that if any illness afflicted these individuals during their medical school careers we could determine the effect of such illness on spermatogenesis and also, if inhibition of the latter took place, to determine the kinetics of the inhibition and recovery, if any. This study has been most successful⁶ in many ways, but the 3 cases I am about to quote have given us important information not only about the effect of certain illnesses on sperm production, but also upon the time processes involved.

CASE REPORTS

Case 1 A medical student (age 25 years) of normal physique and unimportant medical history. Semen quality excellent over a period of 3 years and observed at regular intervals for several months prior to an attack of chickenpox. Course of disease entailed a spiking fever for 5 days, ranging from 101°F on admission, 99 to 100.5°F on second day, 100 to 102.5°F on fifth and sixth days. Discharged with normal temperature on the eighth day. No complications ensued. His semen

⁶ MacLeod, J. J. Fert. and Steril. In press.

was not examined for nearly a month thereafter, at which time a severe depression in sperm count and motile activity and an increase in the number of abnormal forms were observed. The return of the sperm count to control levels was rapid. Within 18 days after the low count reading, the sperm count/cc had risen to 112 millions and four days later was well beyond the control level. Along with the increase in count the motile activity and the morphology of the cells returned to normal.

Case 2 Well developed, well nourished young male aged 22 admitted to hospital with chickenpox. His temperature upon admission was 103.5F. During the next 3 days his temperature fell steadily and he was afebrile on the fourth day. He was discharged on the eighth day, no complications having ensued.

His semen had been examined in my laboratory 2 years previously and found to be of good quality in every respect. Ten days after his discharge, he submitted a semen specimen for examination at which time the sperm count showed a perceptible drop from the control level. Thereafter, specimens were examined at intervals from 3-6 days, the count falling steadily until it reached the lowest level of 3 million/cc 25 days after his discharge from the hospital. Along with the fall in count, the motile activity of the cells was severely affected and relatively large numbers of abnormal forms appeared. On the twenty-fifth day following his discharge, the poorest semen quality was found, characterized not only by the low sperm count but an almost complete absence of motility and extremely high percentage of abnormal forms. Three days later, while no rise in the sperm count was perceptible, there were definite signs that a new generation of spermatozoa had been formed. In this brief period of 3 days, the motile activity returned almost to the normal level with a high percentage of active cells and the abnormal forms had disappeared. Eight days later (33 days after discharge) the sperm count had increased to 20 million/cc and the motile activity and morphology remained good. Thereafter, the count progression was slow. On the fifty-third day after discharge, the count had reached only 30 million/cc. Another specimen was not seen for 2 weeks, at which time the count had jumped to 211 million/cc with excellent motile activity and morphology. No specimens were seen thereafter.

Case 3 Medical student 23 years old admitted to hospital with complaint of chest pain of 12 hours duration and blood-streaked sputum. Temperature of 104F the previous day. Acutely ill upon admission with severe left pleuritic pain. On aureomycin for three days at which time staphylococcal pneumonia with empyema was diagnosed. Then put on massive antibiotic therapy—10 million units of penicillin every two hours and aureomycin 2 grams daily. Throughout the three weeks of his illness his fever ranged between 99.5F and 104F. He was afebrile during the third hospital week and on the twenty-fourth hospital day penicillin was discontinued though the aureomycin was continued. He was discharged on the thirtieth hospital day.

His semen had been examined in my laboratory 2 years previously and found normal in every respect. Eight days after his hospital discharge he presented a semen specimen at which time only 2 million sperm/cc were found. They had

no motile activity and only 42 per cent of the cells were of normal structure. Thereafter, semen specimens were examined at alternate intervals of 4 and 3 days. Five days later only a very occasional, immotile cell was found with a great increase in abnormal forms. Eight days later no spermatozoa were present. A week later, or 28 days after his hospital discharge, feebly motile cells appeared in the specimen, all of which showed very poor morphology characterized by extreme tapering or completely amorphous forms in equal proportions. About 10 per cent of the cells were of the "megalo" type. No normal forms were present. Four days later, the count was 3 million/cc. The cells still showed feeble motile activity but 8 per cent of them were of normal morphology, the remainder being of the megalo, tapering and amorphous forms. Three days later (35 days after discharge) the sperm count remained low (5 million/cc) but there was a definite improvement in the motile activity of the cells and in their morphology. The percentage of "megalo" cells remained high, the tapering and amorphous cells diminished in number and 30 per cent of the cells were normal. A week later no perceptible change in the sperm count or motile activity was observed but the number of normal forms continued to rise. This "steady state" of count and motility followed for another week (49 days after discharge) but four days later (53 days after discharge) the sperm count rose sharply to 25 million/cc with a corresponding increase in the quality of motility. The morphology remained constant at a level still considerably below normal. One week later (60 days after discharge) the sperm count rose abruptly to 152 million/cc with normal motile activity. At this time, the morphology was normal.

I believe these are the first well-controlled cases recorded in which the effects of illness on spermatogenesis have been followed in such fashion that the kinetics of the inhibition and recovery are known precisely. One would not consider that such a mild disease as chickenpox would have such a profound effect on sperm production. It is easier to understand the effects on sperm production of the severe illness of the third case. What are the possible mechanisms involved? The common features of the three cases quoted here—the disease state itself, the febrile state induced by the disease and the use of antibiotics. There is no evidence as yet in the literature to show that bacteria or viruses *per se* have any inhibiting effect on spermatogenesis. Nor is there any suggestion that penicillin or aureomycin affect the germinal epithelium. We hope to settle the latter point in the near future. But we do have clean-cut evidence that the febrile state in the human male can depress sperm production. Several years ago Hotchkiss and myself showed that if the body temperature was elevated artificially to approximately 104°F for 1½ hours, a severe depression of sperm production followed after a latent period of about 10 days. This confirmed the classic studies of Moore and his co-workers on lower mammals.¹ Though the depressions of spermatogenesis recorded by this method were not so severe as those we have just demonstrated as induced by disease, the time relationships are somewhat similar. After the heat inhibition is applied, the sperm counts reach their lowest

¹ MacLeod, J. and Hotchkiss, R. S. *Endocrinology*, 23: 780, 1941.

² Moore, C. and Oslund, R. *Am. J. Physiol.*, 67: 595, 1924.

level about 30 days later, remain low for about two weeks, and then slowly rise to the control level. As closely as we can calculate in the 2 cases of chickenpox, assuming the elevated body temperatures to be the inhibiting factor, the lowest sperm count levels were reached between 30 and 40 days after the first elevation of temperature and were maintained at this low level for about 2 weeks. In this respect, and lacking knowledge of the effects of the infecting agents *per se* on spermatogenesis, we can assume for the moment that the febrile state is responsible for the inhibition.

In the pneumonia case, however, the circumstances are somewhat different. The patient was acutely ill for at least 2 weeks and high body temperatures prevailed throughout this period. Furthermore, there are debilitation factors in this illness which were not present in the chickenpox cases. The extent of the depression of the sperm count and the extended period of recovery process may be a reflection of the additional stress placed upon this individual. The first semen specimen was seen about 17 days after the acute stage of the illness. At this time, the count was exceedingly low (2 million/cc). Four days later no cells were present, so that absolute sterility can ensue as a result of illness. Recovery was slow, much slower than in the chickenpox cases. It is most interesting to note that during the slow recovery process, the new generation of cells showed a high degree of abnormality which gradually disappeared as more and more cells were produced. Another point of theoretical as well as practical importance is that the latter stages of recovery are most abrupt. This is true too in the chickenpox cases. It can be calculated that the complete cycle of depression and recovery of spermatogenesis in the pneumonia case is about 80 days, or more than $2\frac{1}{2}$ months.

It is clear that illnesses, mild or severe, can produce temporary male sterility but it is just as evident that the chances in favor of recovery of fertility in these cases are excellent. We have no sound reason to believe that male infertility as we know it is due to the various maladies man is likely to encounter after puberty. My personal conviction at the moment is that the poor pattern of spermatogenesis we find in the infertile male which manifests itself in low sperm counts and spermatozoa of generally poor quality, is a pattern laid down in that individual at a very early stage of his development, probably in the embryo. It is a deficient pattern which is not likely to be changed easily by any therapy at our disposal now, or any likely to come along in the near future. This picture is unduly pessimistic, perhaps, but caution rather than optimism will benefit the medical profession and the layman far more than some of the unjustified claims made from time to time.

KIDNEY AND HYPERTENSION

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The American Urological Association has honored me by your invitation to deliver the Ramon Guteras Lecture for this year. The list of Guteras lecturers is a distinguished one and I am proud to have my name added thereto. I accepted your invitation in the belief that it constituted a recognition of the contributions which our research group* in the Department of Physiology of the University of Illinois College of Medicine has made to the pathophysiology of the kidney and to experimental hypertension during the past twelve years.

The American Urological Association rightfully honors Dr. Ramon Guteras. Dr. Guteras was a distinguished surgeon, author, and teacher of urology. He was a brother of one of the liberators of Cuba. Dr. Guteras was also an explorer and big game hunter. He was likewise an amateur boxer of unusual skill and on separate occasions was in the ring with John L. Sullivan and with James J. Corbett. Dr. Guteras was one of the founders of the American Urological Association and was its President for the first three years. Accordingly, the Association shows wisdom in dedicating this lectureship to Dr. Ramon Guteras, explorer, big game hunter, athlete, organizer, scientist, and surgeon.

By hypertension is meant a sustained increase in blood pressure extending over a period of months and years. Hypertension, like fever and leukocytosis, is a sign of disease and not a disease in itself. It is simply one manifestation of an underlying disease process, and a common one, since approximately 15,000,000 people in the United States are estimated to have hypertension. The incidence of hypertension increases steadily from the third decade of life, being less than 5 per cent for individuals under 40 years of age and more than 20 per cent for those beyond 40. Five per cent or slightly more of patients with hypertension have their increased blood pressure on the basis of a known, although incompletely understood, cause. The vast majority, or approximately 95 per cent, have their hypertension as the result of unknown cause or causes. This great group of hypertensives are said to have essential hypertension, which accordingly is equivalent to the term, "fever of unknown origin." For the present, a better term than essential hypertension is hypertensive vascular disease since this emphasizes the basic pathophysiologic condition rather than one of its measurable signs.

The Ramon Guteras lecture given at annual meeting, American Urological Association, Chicago, Ill., May 23, 1951.

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HYPERTENSIONS OF KNOWN CAUSE OR CAUSES

The known causes of hypertension for the five per cent of patients with this sign of disease are best classifiable into renal, cerebral or neurogenic, endocrine, and cardiovascular

a) *Renal hypertension* Although a role for the kidney in the pathogenesis of hypertension was suspected for many years, the first definitive proof of this fact was the classic experiment of Goldblatt in which he showed that constriction of the renal arteries of the dog produced hypertension. This experiment has now been repeated in a number of species of animals and it has also been shown that a figure-of-eight tie compressing the kidney or a cellophane or silk bag resulting in the encapsulation of the kidney in a perinephric membrane act similarly to constriction of the renal arteries in producing hypertension. Unfortunately the mechanisms whereby partial constriction of the renal arteries produces hypertension in experimental animals have not yet been determined with certainty. It is usually assumed but not proved that moderate renal ischemia is necessary to set off the pressor mechanism of experimental renal hypertension, certainly some pathogenetic alteration in renal hemodynamics occurs following partial constriction of the renal arteries. Experimental renal hypertension has been ascribed to the secretion of renin by the kidney, to a decreased secretion of a depressor or blood pressure regulating hormone by the kidney, and to an increased formation of pressor amines by the kidney. None of these three concepts has been proved with certainty, although there is suggestive evidence for each. The most cogent evidence to date favors renin as the pathogenetic agent of experimental renal hypertension. This evidence is based on the production of an antibody or antihormone to hog renin in the dog (antirenin) which our research group first suggested ten years ago was effective in preventing the development of experimental renal hypertension and in reducing the blood pressure of renal hypertensive dogs to normotension. We now have conclusive evidence that a sufficient titre of antirenin to hog renin in the dog is highly effective prophylactically and therapeutically against experimental renal hypertension in this species.¹ Unfortunately, while antirenin to hog renin produced in the dog and other species neutralizes the indirect pressor effect of hog, dog, and a number of other animal renins, it does not neutralize human renin. For the present, then, renin-antirenin therapy is not available for trial in human hypertension of renal origin. These findings have been confirmed by Goldblatt and coworkers* and by Helmer, Shipley and coworkers.² However, the semi-purified hog renins employed in these experiments to date are not pure and their contamination with at least two other renal vasoactive agents, viz ,

¹ Wakerlin, G. E., Osgood, B. G., Bird, R. B., Brannick, T. L., Moore, J. B., Burns, R. O., Hawthorne, E. W., and Sevy, R. W. Treatment and prophylaxis of experimental renal hypertension with renin. Trans. Fourth Conference on Factors Regulating Blood Pressure, Josiah Macy, Jr. Foundation, 1950, New York, N. Y.

² Goldblatt, H. Trans. Fifth Conference on Factors Regulating Blood Pressure, Josiah Macy, Jr. Foundation, 1951, New York, N. Y. (In press.)

* Helmer, O. M. Trans. Fifth Conference on Factors Regulating Blood Pressure, Josiah Macy, Jr. Foundation, 1951, New York, N. Y. (In press.)

so-called sustained pressor substance (SPS)⁴ and vaso-excitatory material (VEM),⁵ to which we have shown antibodies to be produced, leaves the renin pathogenesis of experimental renal hypertension still somewhat open. Hass and Goldblatt⁶ have very recently produced a hog renin of great but not absolute purity (5000 D U per mg N), further work with hog renin of this and still greater purity should soon settle the problem. Our research group⁷ and Grollman and coworkers⁸ have shown that experimental renal hypertension in the dog will respond to an unknown principle which is variously and inconstantly present in certain fish liver oils and fractions and concentrates thereof. This substance has the advantage of being effective by mouth. Unfortunately, in the past few years available amounts of this agent have been insufficient even for animal experimentation. Interestingly enough, our research group has shown that the blood pressure of renal hypertensive dogs can also be lowered without any toxic effects by means of the pressor and vasoconstrictor amine, pareдрine, orally administered.⁹ As with the previous treatments mentioned, the blood pressure decrease from pareдрine requires some weeks of therapy with a gradual return toward the original hypertensive level over a period of months following cessation of therapy. The mechanism of the amine antihypertensive action is unknown. At present a search is being conducted for amines which might be antihypertensive without showing any temporary pressor effect during the initiatory period of treatment. None of these promising therapeutic leads for experimental renal hypertension, as previously stated, is present beyond the laboratory stage. Trial in human hypertension must await further work in experimental animals and at the present time would be premature.

Since the report of Goldblatt, a small number of patients have been found in whom nature by one means or another has performed an experiment similar to that of renal artery constriction by a silver clamp or of renal compression by a tie or perinephric membrane. Renal vascular anomalies and obstructions to the renal circulation, as well as affections of perinephric structures, such as perinephritis, tumors, and other masses causing pressure on the renal parenchyma, have been responsible for hypertension. Although the mechanisms producing the hypertension in these patients are presently unknown, they may very well

⁴ Shuplev, R. E. and Helmer, O. M. The presence in blood of a principle which elicits a sustained pressor response in nephrectomized animals. *Trans. of the Second Conference on Factors Regulating Blood Pressure*, Josiah Macy, Jr. Foundation, New York, N. Y., 1948.

⁵ Shorr, E. Comparative study of experimental renal and human essential hypertension with respect to the participation of the hepatorenal vasoactive factors, VEM and VDM. *Fourth Conference on Factors Regulating Blood Pressure*, Josiah Macy, Jr. Foundation, New York, N. Y., 1950.

⁶ Hass, I., Lamfrom, H. and Goldblatt, H. Purification of renin and production of antirenin in man. *Fed. Proc.*, 10: 193, 1951.

⁷ Moss, W. G. and Wakerlin, G. E. Vitamin A concentrates, marine oil fractions, and vitamin K in the treatment of experimental renal hypertension. *J. Pharm. & Experimental Therap.* 85: 355-358, 1946.

⁸ Grollman, A. Experimental chronic hypertension. Its mechanism and amelioration by use of various blood pressure reducing substances, *Spec. Pub.*, New York Acad. of Science, vol. 3, 1945.

⁹ Oller, I. A. and Wakerlin, G. L. Further studies on the treatment of experimental renal hypertension with pareдрinehydrobromide. *Fed. Proc.*, 7: 87-88, 1948.

be the same as those pathogenetic in experimental renal hypertension in animals. Although unilateral renal artery constriction in the dog usually results in only a temporary hypertension (which becomes permanent on contralateral constriction or nephrectomy) a few animals show a persistent hypertension on unilateral constriction. Nephrectomy of the constricted kidney in such animals usually results in a prompt return of the blood pressure to normotensive levels. In the rat unilateral renal artery constriction frequently gives rise to lasting hypertension. If the involved kidney is removed in the first several weeks, the blood pressure usually returns to normal, when nephrectomy is performed some months later, the hypertension is likely to persist, presumably because the opposing kidney has become involved. It might be well here to point out that two weeks in the life of a rat is comparable to one year in man. Stimulated by these experimental findings, unilateral nephrectomy has been performed in a number of hypertensive patients with presumed abnormality limited to the removed kidney. In some of these patients, there was a permanent cure of the hypertension similar to that seen in the dogs and rats described. In many more, however, the decrease in blood pressure was temporary, in some there was no change, and in a minority there was an accentuation of the hypertension following nephrectomy. Too many of the favorable reports in the literature are based on postoperative observation periods of insufficient duration. Here, as in the field of cancer, the final report should be based on a 5 year interval of follow-up. Accordingly and properly, except in those unusual instances where nature has performed a unilateral Goldblatt experiment (an incidence of perhaps one in one thousand hypertensions) and in certain patients with unilateral pyelonephritis and hypertension in which nephrectomy for the cure of the hypertension is justified, hypertension should not be considered as an indication for nephrectomy in man. Rather, urologic considerations should determine whether or not the nephrectomy is to be performed, irrespective of the blood pressure level. Nonetheless, patients with hypertension are entitled to at least a minimal urologic work-up, which should include urinalysis, one of the simpler tests for renal function and, if indicated, excretory urography. These and further urologic studies when warranted by the minimal work-up results, will enable the diagnosis of those rare hypertensions which are on a unilateral nephrogenic basis and accordingly amenable to cure by nephrectomy.

The hypertension of acute glomerulonephritis has been suggested as due to increased secretion of renin but the evidence is highly inconclusive. Evidence for increased vasomotor tonus as responsible for the hypertension is better but not conclusive. The pathogenetic mechanism of the hypertension in chronic glomerulonephritis is presently unknown. As might be expected, the treatment of the hypertensions of acute and chronic glomerulonephritis is relatively unsatisfactory. Attacks of hypertensive encephalopathy may be relieved and the blood pressure temporarily lowered by intravenously or intramuscularly administered magnesium sulfate solution. The hypertension of chronic glomerulonephritis has been treated by sympathectomy, low protein diet, and low salt diet usually, though not always, with indifferent success. The hypertension which may be associated with pyelonephritis results from pathogenetic mechanisms

which are presently unknown although renin and other renal pressor and blood pressure regulating mechanisms may be involved. In the treatment of pyelonephritis eradication of the infecting organism by appropriate antibacterial and antibiotic agents, along with relief of any obstruction present in the urinary tract, is essential. Therapeutic agents should be given in full dosage from the beginning in order to obviate the possible development of a resistant strain of organism. When pyelonephritis is unilateral and renal function tests indicate that the diseased kidney has lost its excretory functions and that the opposite kidney is normal, nephrectomy is indicated and, as stated previously, hypertension if present on a renal basis should be cured.

The hypertensions associated with toxemias of pregnancy and with intercapillary glomerulosclerosis (Kimmelstiel-Wilson disease), are probably on a renal basis but the mechanisms responsible for the hypertensions are presently unknown.

Occasionally obstructive lesions of the urinary tract may give rise to hypertension through back pressure on the renal parenchyma, although the basic pathogenetic mechanisms remain to be determined.

b) *Endocrine hypertensions* Hypertension may occur as a result of pituitary basophilism, adrenocortical tumors, and pheochromocytomas. The mechanisms of the hypertension in pituitary basophilism and adrenocortical tumors are presently unknown, although it is possible that there may be an increased secretion of an as yet unidentified adrenocortical steroid hormone which may have an important pressor effect with minimal effects on salt and carbohydrate metabolisms. In keeping with this concept, the secretion of adrenocorticotropin may possibly be increased in pituitary basophilism. There is evidence, some from our laboratory, suggesting that adrenal cortical steroids may stimulate the renal pressor mechanism, presumably renin secretion, so that these endocrine hypertensions may be partly or even largely renal in origin. Only in the case of the hypertension due to pheochromocytoma do we know the exact mechanism of the hypertension, viz., an increased secretion of the adrenal medullary hormones, epinephrine and nor-epinephrine (adrenalin and nor-adrenalin). Surgical removal of a number of adrenocortical tumors and of pheochromocytomas has resulted in the cure of the hypertensions presented by these patients.

c) *Cardiovascular hypertensions* The term as used here has a specific connotation and is used to refer to the hypertensions which may result from coarctation of the aorta and occasionally from congestive heart failure. The hypertension of coarctation of the aorta is in some patients on the basis of increased resistance due to the aortic constriction. In some patients, however, particularly where the constriction is in the lower thoracic and upper abdominal aorta, a renal factor similar to that of experimental renal hypertension may be involved. This is suggested by the experiment of Goldblatt in which constriction of the aorta of the dog above the origin of the renal arteries resulted in hypertension whereas constriction below the renal arteries did not produce hypertension.¹⁰ Recently, as you know, surgical excision of the area of coarctation has been

¹⁰ Goldblatt H., Kahn, J. R., and Hanzal, R. F. Studies on experimental hypertension. IX. The effect on blood pressure of constriction of the abdominal aorta above and below the site of origin of both main renal arteries. *J. Exp. Med.*, 69: 649, 1939.

successful in some patients with resulting reductions in blood pressure. Some patients with congestive heart failure show increased blood pressure probably as a result of increased venous back pressure on the renal parenchyma with interference to the renal circulation.

d) *Cerebral or neurogenic hypertension* Hypertension may result from increased intracranial pressure as a consequence of trauma, tumor, or inflammation, it may also result from lesions of the diencephalon and/or the brain-stem. The mechanism of the hypertension here is not known with certainty, although increased vasomotor or vasoconstrictor tonus of the sympathetic division of the autonomic nervous system is undoubtedly present. However, our research group has evidence in dogs that increased tonus of the vasomotor system including renal vasoconstriction may set off the renal pressor systems including renin. Accordingly, it is not impossible that so-called cerebral or neurogenic hypertension may have a renal pathogenetic basis, at least in part.

In closing this portion of our discussion concerning hypertension of known causes, it should be emphasized again that differentiation of these hypertension from essential hypertension or hypertension of unknown cause or causes is most important. This is so, because in some of the former patients a complete cure of the hypertension is possible, whereas our therapy of essential hypertension is less satisfactory. Thus, as already stated, when a unilateral renal anomaly, renal tumor, or unilateral pyelonephritis is responsible for the hypertension, nephrectomy may be curative, surgical removal of certain adrenocortical tumors and of pheochromocytomas has resulted in cure of hypertension, and hypertension has been relieved by removal of coarctation of the aorta.

HYPERTENSION OF UNKNOWN CAUSE OR CAUSES (ESSENTIAL HYPERTENSION)

Ninety-five per cent of patients with hypertension belong to this group as previously stated. In spite of the fact that we are yet ignorant of the pathogenetic mechanisms underlying this classification of hypertension, the past 20 years have been highly fruitful in advancing our knowledge of the condition and it is not too much to expect that the present decade may bring us sufficient understanding on which to base a specific, efficient therapy. Accordingly, we shall review the more important recent advances in this field from the standpoint of etiology, pathophysiology, pathogenesis, and treatment, particularly with regard to the possible relation of the kidney.

a) *Etiology* Recent studies have confirmed the facts that essential hypertension, or hypertensive vascular disease, appears more frequently in certain families and in stocky, pyknic, overweight individuals. However, heredity and body type must operate through pathophysiologic mechanisms which it is up to us to determine.

b) *Pathophysiology or hemodynamics* In ordinary, uncomplicated essential hypertension, the cardiac output is normal, the blood volume is normal, the viscosity of the blood is normal, and in early hypertension the elasticity of the arteries is more or less within normal limits for the particular age group of the

patient The factor responsible for the increased arterial blood pressure is the augmented peripheral resistance in the systemic vascular tree due to narrowing of the lumina of the arterioles A greater head of pressure is necessary to force the blood through the narrowed arterioles into the capillary circulation In early essential hypertension the arteriolar narrowing results from generalized arteriolar vasoconstriction, but as the hypertensive process continues, the augmented peripheral resistance becomes partially due to progressive arteriosclerosis which becomes notably present in the kidneys, spleen, pancreas, liver, and brain in decreasing order of intensity Hypertension also appears to accelerate the progress of atherosclerotic changes in the larger arteries, including the aorta, the coronaries, and the cerebral arteries

The work of the heart is increased in hypertension and roughly in proportion to the systolic pressure As the hypertension continues the left ventricle of the heart hypertrophies but the coronary blood supply tends to lag behind Since the hypertensive heart functions at a higher than normal base, it possesses a distinctly reduced reserve Moreover, as already indicated, the coronary arteries of hypertensives show a higher incidence of atherosclerosis than normotensives of similar age groups These facts constitute the pathophysiologic bases for the cardiac complications of myocardial insufficiency and infarction

The cerebral arteries have thin walls and are poorly supported by brain tissue since they lie in the perivascular spaces Next to the coronary arteries and the aorta, the cerebral arteries are most subject to atherosclerosis The arterial branches supplying the region of the internal capsule are especially thin-walled and in direct line with the pressure wave from the heart These facts form the pathophysiological bases for the frequency of cerebral hemorrhage in hypertension

With the passage of years progressive renal arteriosclerosis causes a gradual decrease in renal function, although in the great majority of essential hypertensives renal function is still comparatively satisfactory when the hypertension is terminated by death from cardiac insufficiency or infarction, apoplexy, intercurrent disease, or old age However, approximately ten per cent of essential hypertensives succumb to renal failure So-called malignant hypertension may be present from the start, or benign hypertension may suddenly change into the malignant form Most probably, malignant hypertension is a greatly accentuated, accelerated form of benign essential hypertension, although some investigators in this field believe that malignant hypertension differs qualitatively as well as quantitatively from benign essential hypertension The typical lesions of malignant hypertension, viz, arterio- and arteriolonecrosis, involve the renal as well as other systemic artery branches and arterioles, the renal vascular lesions giving rise to renal insufficiency with death in uremia

c) *Pathogenesis* From the standpoint of pathogenesis, essential hypertension is probably a generic classification The hypertensions due to pheochromocytomas, adrenal cortical tumors, and renal abnormalities were once classified under essential hypertension As our knowledge increases, other species of hypertension may be split off Current research on the pathogenesis of essential

hypertension or hypertensive vascular disease, which is a better term, points to renal, neurogenic, and endocrine factors

Renal The classic method of Goldblatt, viz, partial constriction of the renal arteries, produces a hypertension in animals which in many respects resembles essential hypertension This is likewise true for the production of a perinephric membrane in animals and for compression of the kidneys by a figure-of-eight ligature Accordingly, attention has been focussed on the possibility of pathogenetic involvement of the kidney in essential hypertension Unfortunately the mechanisms whereby constriction of the renal arteries produces hypertension in the experimental animal have not yet been determined with absolute certainty, as discussed in the first part of this presentation However, our research group is now developing a technique which we hope will enable us to determine whether the percentage of patients with essential hypertension who have their hypertension on a renal, renin basis is 0, 10, 50, or even 100 per cent As you may know, on the basis of inadequate evidence, Smith and coworkers¹¹ support the first figure viz, 0 per cent, whereas, Goldblatt and associates¹² and E Braun-Menendez and collaborators¹³ favor the last figure viz, 100 per cent The technique which we intend to use is based on the following premise Not only have we been able to produce antihypertensive effects in experimental renal hypertension in dogs by active immunization with hog renin but we have also obtained similar effects in renal hypertensive dogs by the passive administration of dog antiserum containing antirenin to hog renin¹⁴ Since only antirenin to human renin will neutralize the pressor effect of human (and monkey) renin, we are now preparing human renin with a view to obtaining antirenin to human renin by injections of human renin into the horse After this procedure is thoroughly worked out in monkeys to avoid possible injurious effects, we hope to study a group of essential hypertensives to determine whether a sufficient quantity of purified antirenin to human renin passively administered will significantly reduce the blood pressure¹⁵ So far as we are aware, this is the only method presently available for determining the proportion of essential hypertensives who may have their hypertension on a renal, renin basis

Neurogenic A certain portion of essential hypertensives show a significant reduction in blood pressure when subjected to sedation or to general anesthesia This is also true for spinal anesthesia which blocks the preganglionic vasoconstrictor fibers, or tetrathylammonium chloride which blocks autonomic ganglia, and dibenamine which paralyzes vasoconstrictor nerve endings in the arteriolar wall Likewise, some patients show lasting reductions in blood pressure from sympathectomy These findings suggest but do not prove that a group of es-

¹¹ Goldring, W and Chasis, H Hypertension and Hypertensive Disease Commonwealth Fund, New York, N Y, 1944

¹² Goldblatt, H The Renal Origin of Hypertension C C Thomas, Springfield, Ill, 1948

¹³ Braun Menendez, E Personal communication, 1950

¹⁴ Brannick, T L, Osgood, B G, Burns, R O and Wakerlin, G E Treatment of experimental renal hypertension with antirenin Am J Physiol, 163 701, 1950

¹⁵ Wakerlin, G E, Osgood B G Bird, R B, Brannick, T L, Moore, J B, Burns, R O, Hawthorne, E W and Seely, R W Treatment of experimental renal hypertension with renin and with antirenin J Lab & Clin Med, 36 1002, 1950

essential hypertensives have their increased blood pressure primarily on the basis of augmented vasoconstrictor nerve activity. This may in turn be due to increased tonus of the medullary vasomotor center consequent upon corticohypothalamic imbalance (nervous tension). It is also obvious that protracted vasoconstriction involving the renal area may release renal pressor mechanisms and introduce a complicating renal factor into the mechanism of this neurogenic component. In any event, many patients with essential hypertension show a neurogenic component, even though their hypertensions may ultimately prove to be on other pathogenetic bases.

Endocrine On the experimental side, the maintenance of experimental renal hypertension is dependent upon adequate anterior pituitary and adrenal cortical functions. On the clinical side, a minority of patients with essential hypertension show an increased tolerance to insulin, large doses of desoxycorticosterone have produced hypertension in normotensive humans, sodium chloride metabolism is mildly altered in essential hypertension, and marked sodium chloride restriction has an antihypertensive effect in some essential hypertensives. These findings suggest but do not prove that a certain undetermined proportion of patients with essential hypertension may have increased adrenal cortex function as the pathogenetic basis for their elevated blood pressure. The adrenal cortex may differentially produce an augmented secretion of an as yet unknown cortical steroid with a predominant vasoconstrictor effect and with minimal effects on carbohydrate and salt metabolisms. There is some evidence suggesting that this adrenocortical vasoconstrictor effect may be indirect and may involve activation of a renal pressor mechanism, so that here again we come back to the kidney.¹⁶

Treatment There is no magic bullet for the treatment of essential hypertension. In this thumbnail sketch of therapy for uncomplicated essential hypertension, it is important to emphasize that psychotherapy is an important adjunct and that intermittent courses of the barbiturates will remove some of the nervous tension. Certain drugs which are capable of blocking vasoconstrictor nerve impulses are being tested in the treatment of essential hypertension, but the results, in my judgment, are not particularly promising. The nitrites, nitrates, and xanthines are of value in the treatment of angina as a complication of essential hypertension but of questionable value for the hypertension itself. Thiocyanate therapy is controversial and somewhat on the wane. Recently, a low protein, low salt diet consisting principally of rice and fruit has been recommended on the thesis that the kidney is involved pathogenetically in essential hypertension and that the work of this organ is reduced by the low protein, low salt diet. The rice diet probably produces its effect through its low salt component. Recent studies have shown that about 10 per cent of essential hypertensives obtain a good result from a low salt diet. Sympathectomy appears to be curative in about 10 per cent of patients with essential hypertension, although the criteria presently available are not too satisfactory in differentiating patients who will obtain an excellent result from those who will not.

¹⁶ Bergerer, H. F. and Waterlin, G. E. Relation of the adrenal glands to the renin concentration of the canine kidney. *Am. J. Physiol.*, 155: 426, 1948.

CONCLUSIONS

The determination of the causes, pathophysiology, pathogenesis, and more effective treatment of the various forms of hypertension, including most importantly essential hypertension, requires further medical and biological research, inclusive of animal experimentation. The fact that our research group and others have recently developed successful therapies for experimental renal hypertension and for experimental malignant hypertension in animals¹⁷ suggests the possibility that more successful therapies for human benign and malignant hypertension may be achieved even within the present decade.

¹⁷ Burns, R O, Osgood, B G and Wakerlin, G E. Prophylaxis of experimental renal malignant hypertension with crude and semi-purified hog renins. Fed Proc, 10 22, 1951

UROLOGIC ASPECTS OF ARTERIAL HYPERTENSION

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Richard Bright,¹ in 1827-36, is credited with the first observation relating arterial hypertension to disease of the kidneys in man. Although he had no means of determining the blood pressure, he demonstrated abnormal resistance to injections offered by the renal arteries of those patients who died with enlarged and thickened hearts in whom there was no local disease of the heart to explain the hypertrophy.

In 1909 Janeway² produced moderate sustained hypertension in two dogs by ligation of branches of both renal arteries. In 1932 Chanutin and Ferris³ produced sustained hypertension in a large series of rats by partial removal of one kidney and subsequently total removal of the other. Hypertension was sustained in some rats for as long as seven months.

The classic experimental work of Goldblatt⁴ in producing persistent elevation of blood pressure in animals by partial constriction of the main renal artery has evoked great interest and a large series of publications.

Few fail to accept the renal origin of hypertension associated with glomerulonephritis (acute and chronic), bilateral chronic pyelonephritis, bilateral polycystic disease of the kidneys, bilateral ureteral obstruction, renal amyloidosis and other conditions that involve considerable reduction of renal parenchyma.

Essential hypertension by definition has been characterized as elevated blood pressure of unknown origin without recognizable disturbance of renal excretory function, in the early phase. It is in so-called essential hypertension that the primary renal origin of the elevated blood pressure is still held in doubt.

Goldblatt's idea of producing hypertension by a disturbance of intrarenal hemodynamics was based primarily upon the observation that intrarenal stenosing arterial and arteriolar sclerosis is found with great frequency in both the benign and malignant phases of essential hypertension, together with the clinical and experimental evidence that hypertension can be produced by renal disturbances. There was then and there still is no known way to reproduce the intrarenal anatomic abnormality, namely, arterial and arteriolar sclerosis localized to the kidneys. His procedure of permanent constriction (not occlusion) of the main renal artery with a clamp was a compromise. It does not mean that stenosing arteriosclerosis of the main renal artery is considered to reproduce exactly the anatomical state of the kidney in hypertension. This incorrect interpretation has been made by a number of authors and investigators.

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¹ Bright R. *Guss's Hospital Rep.*, 1: 338, 1836; Janeway, T. C. *Proc Soc Exp Biol & Med.*, 6: 102, 1927; Chanutin, A. and Ferris, E. B., Jr. *Arch Int Med.*, 49: 767, 1932.

² Goldblatt, H. *Am J Med.*, 4: 100, 1948.

There have been three acceptable instances of the renal genesis of hypertension due to main renal artery obstruction reported by Leadbetter and Burkland,³ Prinzmetal,⁴ and Saphir.⁵

Goldblatt found that constriction of the main renal artery of only one kidney was sufficient to induce a rise of blood pressure. In the dog, the elevated blood pressure usually lasts from four to six weeks. Removal of the one kidney, with the main renal artery constricted, results in a prompt return of blood pressure to normal.

Constriction of both main renal arteries results in permanent elevation of blood pressure. The same effect is produced by constriction of one main renal artery and contralateral nephrectomy. By this means persistent hypertension has been produced in animals and the blood pressure has remained elevated in some dogs for more than six years. In these animals with persistent hypertension due to moderate constriction of both main renal arteries there was no significant alteration of renal excretory function.

If both main renal arteries are greatly constricted from the start, or, if moderate constriction is practiced at first and greater constriction later, hypertension accompanied by variable degrees of impairment of renal excretory function results. The same effect can be produced by excessive constriction of one main renal artery with contralateral nephrectomy or contralateral ureteral occlusion. In those animals that develop great impairment of renal excretory function along with hypertension, fatal convulsive uremia occurs and, at autopsy, the small arteries and arterioles in many organs show pathologic changes which resemble those observed in malignant phase of essential hypertension, i.e., acute necrotizing arteriolitis.

It seems clear that in the experimental animal, made hypertensive by partial occlusion of the main renal artery, that the rise in blood pressure is of humoral rather than nervous origin. Most investigators agree that a chemical agent of renal origin is the probable cause of the elevated blood pressure in experimental renal hypertension. Renin has been accepted by many investigators, as the name of the basic principle of this chemical agent.

Renin has been demonstrated in the systemic blood in the acute phase of experimental benign renal hypertension, in the malignant phase of experimental renal hypertension, and in some forms of hypertension associated with renal disease in man, i.e., acute glomerulonephritis. However, it has not been demonstrated that renin in appreciable quantities exists in the systemic blood of animals in chronic benign phase of experimental renal hypertension, or in human beings in the benign or malignant phase of essential hypertension.

In addition to renin, a number of other humoral mechanisms have been suggested as playing a role in essential hypertension. Perhaps the most promising lead in this regard has resulted from the work of Shorr and his associates.⁶ They have detected a vasodepressor (V D M) and a vaso-excitor material (V E M).

³ Leadbetter, W. F. and Burkland, C. E. *J. Urol.*, 39: 611, 1938.

⁴ Prinzmetal, M., et al. *J. A.M.A.*, 118: 44, 1942.

⁵ Saphir, O. and Ballinger, J. *Arch. Int. Med.*, 66: 541, 1940.

from the blood of patients in a state of shock, essential and renal hypertension suggesting that the interaction of these two substances may be of importance in setting the level of the blood pressure

In two recent books^{7, 8} on the subject of hypertension, divergent views were expressed about the mechanism of elevation of the blood pressure, indicating that the role of the kidney in essential hypertension is still unknown

Although most investigators believe that the vascular changes in the kidneys are secondary to the hypertension, the evidence for this still is inconclusive and the final answer will depend on the study of adequate kidney biopsy material in early phases of the disease. The urologist is in the unique position of being able to gather and correlate this type of information by routinely taking biopsy material during operations which require opening the parenchyma of the kidney

Since studies of experimental hypertension are inconclusive regarding the role of the kidney in human hypertension, except perhaps, in acute renal disorders such as acute glomerulonephritis, it seems worthwhile to re-evaluate the clinical evidence concerning the association of hypertension and renal disease, both unilateral and bilateral

THE INCIDENCE OF HYPERTENSION

Master,⁹ using a blood pressure of 150/90 as the upper limit of normal, estimated from an analysis made in 14,849 people of age 40 years and above, that one-half of the male population and 60 per cent of the female population of forty years and over are hypertensive

Brausch,¹⁰ using a blood pressure of 150/90 as the criterion, estimated that 25 per cent of persons 30 years and older, and increasing to 60 per cent in elderly persons, have hypertension. His study was based on 975 consecutive patients taken at random from registration at the Mayo Clinic

INCIDENCE OF HYPERTENSION IN PATIENTS WITH UROLOGIC DISEASE

Goldring and Chassis,¹¹ in a control group of 2928 living patients, found that 26 per cent of them had hypertension, and in a group of 433 necropsy control patients, an incidence of 26.5 per cent with hypertension was found. In 585 patients with proven unilateral renal disease there were 24.2 per cent with hypertension

Pearman¹² reported that from urographic evidence the incidence of hypertension was no greater in patients with pyelonephritis than in patients with

⁷ Zweifach, B. W. and Shorr, E. Proc 1st Clin ACTH Conference, Philadelphia Blakiston Co., 1950, p. 289

⁸ Goldring, W. and Chassis, H. Hypertension and Hypertensive Disease. New York Commonwealth Fund, 1944

⁹ Braun Menendez, et al., Translated by L. Dexter. Renal Hypertension, Springfield, Ill., Chas. C Thomas, 1946

¹⁰ Brausch, A. M. et al. J A M A, 121: 1251, 1943

¹¹ Brausch, W. F., Walter, W. and Hammer, H. J. J A M A, 115: 1837, 1940

¹² Goldring, W. and Chassis, H., Hypertension and Hypertensive Disease. New York Commonwealth Fund, 1944, p. 114

¹³ Pearman, R. O. et al. Proc Staff Meet., Mayo Clinic, 15: 467, 1940

nonrenal disease In a series of 500 patients with pyelonephritis, either unilateral or bilateral, there was a 9 per cent incidence of hypertension, in 500 patients with goiter without hyperthyroidism there was 10 per cent, and in 500 patients with gallbladder disease there was a 7 per cent incidence of hypertension

Hines¹² reported among 264 patients with urologic disease, who were observed over a period averaging 15 3 years, the incidence of hypertension either prior to or subsequent to the first observation was practically identical with a control series of 790 patients without urologic disease

Braasch, Walters, and Hammer,¹⁰ and Baggenstoss and Barker¹⁴ record a high incidence of hypertension in unilateral pyelonephritic atrophy and unilateral pyonephrotic atrophy They believe that a causal relationship is indicated by these statistics

Smith¹⁵ concluded that with the possible exception of pyelonephritis and pyonephrotic atrophy the available data did not indicate that urologic disease increased the incidence of hypertensive disease, or that it in any large number of instances was causally related to its genesis

INCIDENCE OF UROLOGIC DISEASE IN HYPERTENSION

The incidence of urologic disease as determined by pyelographic evidence in hypertensive patients varies from 45 per cent presented by Schroeder and Steele¹⁶ (24 per cent unilateral renal abnormalities) in an analysis of 250 hypertensives, to 8 9 per cent in 2,055 hypertensives as reported by Rathliff and Nesbit¹⁷

Rath and Russek¹⁸ combined the statistics of Palmer and his coworkers, Rathliff and Conger, Braasch, Schroeder, and Steele, and others, and they noted that of a total of 6,044 hypertensive patients, 10 7 per cent exhibited evidence of urologic disease They contrasted this figure to the 27 4 per cent incidence in normotensives reported by Wosika, Jung, and Maher and concluded that the incidence of urologic disease among hypertensives is not greater, and possibly less, than among normotensive subjects

Chassis and Redish¹⁹ in clearance studies of 21 hypertensive subjects selected at random, demonstrated that renal functional impairment proceeds to an equal degree or at a parallel rate in both kidneys

From the available data, approximately 10 per cent of hypertensive patients have demonstrable urologic abnormalities with functional impairment Since the possibility of coincidence is very great, the only way a causal relationship can be demonstrated in any particular case is by "curing" or improving the hypertension by removing the kidney

Smith¹⁵ reviewed the literature and found 242 instances in which unilateral nephrectomy had been performed in association with hypertension He required for a cure that the blood pressure be lowered to or below 140/90, and that it

¹² Hines, E A, Jr and Lander, H H J A.M.A., 116 1050, 1941

¹⁴ Baggenstoss, A H and Barker, N W Arch Path., 32 966, 1941

¹⁵ Smith, H W Am J Med., 4 724, 1948

¹⁶ Schroeder, H A and Steele, J M Arch Int Med., 68 261, 1941

¹⁷ Rathliff, R K, Nesbit, R M, et al J A.M.A., 133 296, 1947

¹⁸ Rath, M M and Russek, H I Am Heart J., 29 516, 1945

¹⁹ Chassis, H and Redish, J Arch Int Med., 70 738, 1942

remain within normal limits for at least one year. A summary of his analysis of these collected cases is shown in table 1.

Smith concludes "We are obliged, tentatively, to accept these 47 patients as 'cures', but nevertheless, it leaves a lingering doubt that the urologic disease was actually the cause of the hypertension." Of these 47 successful cases, 22 were of unilateral pyelonephritis. The age incidence of the successful cases showed 17 subjects under twenty years of age, but 24 were in their fourth or later decade of life.

Ratliff and Nesbit¹⁷ reported 49 cases of severe hypertension in whom nephrectomy was performed. All but 8 of the subjects were followed 12 months or longer. Their results showed 17 cases or 34.6 per cent "cured", 6 cases, 12.4 per cent improved, and 26 cases or 53 per cent failures. Of this group there were 8 patients with pyelonephritis, 11 patients with hydronephrosis, and 7 patients with calculus pyelonephrosis.

Barker and Braasch²⁰ reported a review of 61 patients who came to the Mayo Clinic primarily because of hypertension. All were found to have advanced disease of one kidney and minimal, if any, evidence of disease in the other. All underwent removal of the diseased kidney. Based on a two-year follow-up on the entire series, they reported 25 cases (41 per cent) "good" results—i.e. blood

TABLE 1 *Effects on blood pressure, 242 cases*

NO SIGNIFICANT REDUCTION	REDUCED BUT NOT TO NORMAL	REDUCED TO NORMAL OBSERVATION LESS THAN ONE YEAR	REDUCED TO NORMAL FOR ONE YEAR OR MORE
135 (56%)	43 (18%)	17 (7%)	47 (19%)

pressure 150/100 or less, 10 cases (16 per cent) "fair" results (blood pressure significantly reduced but greater than 150/100, and 26 cases (43 per cent) deaths or no lowering of blood pressure.

Wilson and Byron²¹ and others have observed malignant arteriolar lesions in the contralateral kidney of rats with hypertension caused by constriction of one main renal artery. Goldblatt has not been able to confirm this observation in dogs, rabbits, monkeys, sheep or goats with hypertension due to constriction of one main renal artery. Goldblatt has pointed out that all the glomerular and interstitial inflammatory lesions, as well as the vascular lesions, have been observed within an otherwise supposedly normal rat kidney. He feels that in their rat experiments they may have been dealing with bilateral renal disease. There remains the possibility that the rat may differ in this respect from all other animals.

In spite of the experimental and statistical evidence against the probability of curing hypertension by unilateral nephrectomy there are well documented cases of cures by this procedure.

Subjects suitable for nephrectomy may be divided into three categories:

1) Patients with reliable criteria of cardiovascular disease in which one kidney

¹⁷ Barker, N. W. and Braasch, W. F., *Surg. Gynec. & Obst.*, 84: 200, 1947.

²¹ Wilson, N. C. and Byron, F. B., *Lancet*, 1: 135, 1939.

had insufficient functional ability to support life, and with a normal or compensated contralateral kidney (cases 1 and 2)

During childhood persistent elevation of blood pressure is uncommon and essential hypertension is rare. The majority of such cases are associated with renal disease. The probability of cure by unilateral nephrectomy when unilateral renal disease is present in children is very great.

2) Patients with associated hypertension in which nephrectomy is indicated on sound urologic principles (case 3)

3) Patients who are operated upon "in desperation." These patients should have markedly diminished function in the kidney to be removed and to have shown a continued downhill course in spite of medical and possible psychiatric therapy. These patients may have some functional disturbance in the contralateral kidney (case 4)

CASE REPORTS

Case 1 JS, a 27-year old white, married man, was admitted to Holmes Hospital on November 7, 1948 complaining of blurred vision of 3 weeks' duration.

At the time of his induction into the Army in 1943, it was found that he had a systolic blood pressure of 179, which resulted in his being hospitalized for 1 week in a military hospital. There, his blood pressure was taken t i d, each time after 2 hours of bed rest. His blood pressure averaged 144 systolic during this period of observation, and he was accepted for military duty. He was discharged from the Army in February 1946, without further mention of hypertension. He had no urinary complaints.

Two days before admission to the hospital he consulted a ophthalmologist because of failing vision. The eye grounds showed grade 4 hypertensive retinopathy, fresh hemorrhages, exudate and papilledema, and his systolic blood pressure was recorded over 200. The remainder of the physical examination was negative, except for an apical systolic murmur.

Laboratory examinations showed a normal blood count. The urine was negative, except for an occasional cast and a trace of albumin. The blood urea nitrogen was 10 mg per cent. Urine culture was sterile. He was able to concentrate the urine to 1:025 and the phenolsulfonphthalein secretion showed 35 per cent of the dye secreted in 15 minutes, with a total output of 75 per cent in 2 hours.

Excretory urograms showed a normal left kidney, but no dye secreted on the right side. A right retrograde pyelogram showed a large extrarenal hydronephrosis with a small kidney shadow with very little renal parenchyma. There was obstruction at the right ureteropelvic juncture. The pyelograms were interpreted as showing a compensatory hypertrophy of the left kidney and hydronephrosis of a congenital hypoplastic right kidney due to ureteropelvic obstruction.

The blood pressure response to tetraethyl ammonium chloride (TEAC) was measured on three occasions revealing very slight depressor effects of the drug. Since TEAC blocks the autonomic nervous system, the lack of depressor response

suggested that the blood pressure was maintained by humoral rather than neurogenic tone²²

He was in the hospital 18 days before operation. Blood pressure determinations were made 4 times daily, and showed a variation from 225/170 to 160/120.

On November 29, 1948 a right nephrectomy was performed. A hypoplastic kidney with a large extrarenal pelvis was removed. An aberrant artery was found obstructing the ureteropelvic juncture.

There was no significant drop in blood pressure during the first 7 days following operation. During the next 5 days the blood pressure ranged between 140/100 to 120/90.

Pathological report. The gross specimen consisted of a kidney measuring 10 by 6 by 3 cm. in diameter. The capsule was moderately adherent. Dissection of the vessels revealed the renal vein to appear grossly unremarkable, except that it was slightly smaller than usual. Accompanying the vein, there was one artery which was definitely smaller than the expected renal artery. This artery entered the pelvis with the vein, and appeared to nourish the superior two-thirds of the kidney. At the level of the ureteropelvic junction another small artery was present, anterior to the ureter, and seemed to be nourishing the lower third of the kidney. The pelvis when opened was seen to be extremely dilated, possessing a capacity of at the very least, 45 cc. The wall of the pelvis seemed markedly thickened and fibrotic. Microscopic sections showed a marked diminution in the number of tubules, those persisting being microcystic in type. Only an occasional identifiable glomerulus was seen. In the interstitial stroma, which was scarred, there were only occasional small infiltrations with polymorphonuclear leukocytes and lymphocytes. Rare tubules contained, clustered within their lumens, cells of acute and chronic inflammatory type. The wall of the pelvis showed a marked increase in the amount of collagenous tissue, and in the subepithelial stroma there were relatively few foci of infiltration with chronic inflammatory cells. A striking feature was a severe degree of vascular sclerosis involving vessels of all calibers to an approximate equal degree. **Diagnosis.** Hydronephrosis with marked atrophy of kidney, chronic pyelonephritis, slight, arterio- and arteriolar nephrosclerosis, severe.

The patient has been examined every 3 months since operation. His eye grounds are normal and he is leading a normal life. His blood pressure has ranged between 112/70 to 120/78. The last examination was on September 11, 1950 at which time his blood pressure was 120/78. His urine was normal.

This case is to be reported in further detail at a later date.

Case 2 R M., a 47-year old man, was admitted to Holmes Hospital on March 16, 1949 because of high blood pressure of at least 19 months' duration. Two years ago he had had a subtotal thyroidectomy. Seven months before admission he had had a cerebral accident, the results of which had not entirely disappeared. His eye grounds showed grade 1 retinopathy. The heart was tremendously enlarged. The urine contained 1 plus albumin, 1-2 white blood cells, an occasional red blood cell, and 2-3 hyaline casts. The blood urea nitrogen was

17.3 mg per cent Phenolsulfonphthalein 20 per cent was secreted in the first 15 minutes, with a total secretion of 55 per cent in 1½ hours. Culture of the urine was sterile.

The blood pressure response to tetraethyl ammonium chloride (TEAC) was measured revealing a depressor response. The blood pressure fell from a control level of 225/150 to 150/110, two minutes after the injection. When the blood pressure response was tested with benzodioxane there was no significant response.

Excretory urograms revealed compensatory hypertrophy of the left kidney and no dye appearing on the right side.

The right ureter could be catheterized for only a distance of 1 cm. No urine was obtained from the right ureter. Contrast medium was injected up the right ureter. The right ureter was extremely narrow. The pyelogram showed an extrarenal hydronephrosis with small calyces and almost no renal parenchyma present.

On April 6, 1949, a small, hypoplastic, infantile type kidney was removed. There was no aberrant artery crossing the ureteropelvic juncture. While the pelvis was large and extrarenal in type, it was entirely empty of urine at the time of nephrectomy.

Pathological report. The kidney measured 9 by 8 by 2 cm. The capsule stripped with ease. The cortex was thin and almost absent in the upper pole. The pelvis and calyces were markedly dilated without demonstrable obstruction at the ureteropelvic juncture. An aberrant artery ended in the lower pole of the kidney. On microscopic examination there were seen changes typical of marked atrophy, although one segment appeared functioning. Most of the parenchyma showed profound atrophy, few intact glomeruli and tubules which were thin, dilated, and filled with colloid casts. There was an interstitial infiltration of inflammatory cells of minor degree. There had been atrophy and replacement of tubules and considerable glomerular fibrosis. Intrarenal arteries were markedly sclerotic and narrowed. Major extrarenal vessels were less strikingly involved. **Diagnoses:** 1) Hydronephrosis with slight chronic pyelonephritis, 2) arterionephrosclerosis, severe, with focal cortical atrophy.

There was no improvement in this patient's hypertensive vascular disease following nephrectomy. In general, he has done badly. When last examined on May 24, 1950 his blood pressure was 240/100 and there was a loud systolic apical murmur.

Case S M B, a 43-year old white, married woman was admitted to Bethesda Hospital on August 23, 1947 because of recurring attacks of epigastric pain accompanied by nausea and vomiting. With each episode there was frequency and burning on urination, and pyuria.

Two years before admission she had consulted her family physician because of severe headaches and spells of dizziness. He found that she had hypertension and had treated her for it during this time. Unfortunately no records were kept of the blood pressure readings. She was admitted to the hospital for study regarding the episode of epigastric pain.

When first seen by us the patient had no complaints. Physical examination was essentially normal except for slight tenderness to deep palpation in the left midabdomen.

Urine, blood count, and Kahn test were normal. Cultures of the urine were sterile. Blood pressure was 160/110. Urograms revealed a normal right kidney, but the left kidney was small and there was some blunting of the calyces.

A differential phenolsulfonphthalein test showed the dye to appear from both kidneys in 2½ minutes. During the next 15 minutes the right kidney secreted 30 cc urine with 30 per cent output of phenolsulfonphthalein. The left kidney secreted 7 cc urine with 7 per cent phenolsulfonphthalein. There was no leakage of urine in the bladder during the test.

A left nephrectomy was performed on September 3, 1947. Pathological examination revealed a reddish brown kidney with marked granularity beneath the capsule, which stripped with difficulty. The surface was markedly pitted. The kidney measured 9.5 by 5 by 2.5 cm. The cortex was poorly demarcated from the pyramids and was estimated to be 0.5 cm in thickness. The pelvis was contracted. Microscopic sections showed the parenchyma to be in good part normal in appearance. There was mild to moderate vascular thickening and sclerosis. An occasional focus, however, showed profound atrophy with loss of glomeruli, dilatation and thinning of cast filled tubules, and marked interstitial fibrosis. This was related to interlobular arteries which were sclerotic, occluded, and recanalized. There was little inflammatory reaction. The appearance of the lesion suggested focal ischemia with gradual infarction and atrophy. Diagnosis: Arterionephrosclerosis with focal cortical scarring.

The patient's blood pressure level was recorded as 140/100 in January 1949, 136/80 in June 1949, 122/80 in August 1949, 130/70 in September 1950.

Case 4. C.K., a 58-year old white man was admitted to Bethesda Hospital on June 26, 1948 for study of hypertension. Three years previously he had had a complete medical work-up and no abnormalities regarding his blood pressure or urine were present. Six months before admission he felt below par and had paroxysms of tachycardia. His blood pressure was found to be 170/110 and the urine contained 2 plus albumin. During the next 6 months his blood pressure gradually became more elevated, the albuminuria increased to 3 plus, and for several weeks he had had persistent disabling occipital headaches.

General physical examination was negative. The blood pressure was 190/100. The phenolsulfonphthalein test showed 25 per cent excretion of dye in the first 30 minutes, and a total of 75 per cent in 2 hours. Concentration dilution tests showed the specific gravity of urine to vary between 1.001 and 1.026. Urine albumin 3-4 plus, sugar negative. There was a rare red blood cell, and 2-3 white blood cells. The blood count was normal.

A plain urogram showed multiple calcifications in the spleen and calcifications of blood vessels within the pelvis. X-ray of chest, complete gastro-intestinal series, and barium enema were normal.

Cystoscopic examination of the bladder was normal. Urine from the right kidney contained 4 plus albumin, 8-10 red blood cells, and an occasional granu-

lar cast Urine from the left kidney contained 3 plus albumin, a rare red blood cell, and no casts Phenolsulfonphthalein appeared from the right kidney in 4 minutes with 10 per cent secretion in the first 15 minutes and 10 per cent in the second 15 minutes Phenolsulfonphthalein appeared from the left kidney in 10 minutes, and there was only a trace of dye in 30 minutes There was no leakage of phenolsulfonphthalein in the bladder At the time of the examination the bladder urine contained 4 plus albumin, 12-50 red blood cells, and 0-3 granular casts per high dry field

Retrograde pyelograms were interpreted as compensatory hypertrophy of the right kidney and congenital hypoplasia of the lower two-thirds of the left kidney, with the upper third being normally developed

The eye grounds showed mild sclerotic changes in the retinal vessels, bilaterally

Neurological examination, spinal fluid examination, and x-rays of the skull were normal

Left nephrectomy was seriously considered However, since it was demonstrated that the urine from the right kidney contained 4 plus albumin, it was decided not to perform a nephrectomy as the chances of improving his hypertension did not seem good He was discharged from the hospital for further medical therapy

He was readmitted to the hospital on October 1, 1948 in hypertensive crisis Two days before admission he began to show mental aberrations, nausea, and headache The night before admission he had severe nausea, vomiting with headache all during the night In the morning he had a convulsive seizure with unconsciousness and had been quite dull and lethargic ever since His blood pressure was 210/120 The blood urea nitrogen was 33 mg per cent which dropped to 22 mg per cent 9 days later The urine contained 4 plus albumin, a rare granular cast, a rare red blood cell, and 3-4 white blood cells

On October 14, 1948 a left nephrectomy was performed The blood pressure was 230/110 thirty minutes before the beginning of the anesthetic The left kidney was removed through extraperitoneal lumbar approach There were three aberrant vessels to upper pole of kidney The ureter and pelvis were normal The kidney was one-half normal size The lower two-thirds of the kidney surface was slightly irregular but did not have fetal lobulations It was dark in color The upper fourth of the kidney was normal in color and there was a clear line of demarcation between the two portions of the kidney

Pathological report The kidney weighed 83 gm The capsule stripped with ease and its cortical surface was smooth and glistening The surface was somewhat irregular and contained multiple punctate hemorrhagic areas At one pole the kidney was lighter in color and granular to palpation On section there was sharp cortical pyramidal demarcation The cortex measured 4 mm in thickness at its thinnest portion, 8 mm in thickness in the previously described light colored area The pelvis and calyces were filled with fat, and grossly unremarkable Microscopic examination The sections available, unfortunately, were

taken from relatively intact renal cortex. These exhibited moderate arterio-nephrosclerosis with minor focal cortical scarring. There was no indication of the case of the cortical atrophy observed in the gross. The glomeruli were essentially normal. There was relatively little arterial or arteriolar sclerosis. Diagnosis: Arterio-nephrosclerosis.

The patient has been under frequent and constant observation since operation. Blood pressure determinations have been made two or three times per month. The last examination was on September 15, 1950. Since January 1950, his blood pressure has averaged 157/84. The minimum blood pressure reading was 140/80, and the maximum was 170/90. His urine has contained between 1 and 2 plus albumin. There have been no red blood cells and only a very rare cast in his urine. His hemoglobin is 14 gm. He has been entirely relieved of his headaches and his only complaint has been that he "tired easily." Although it is not necessary for him to work, he works part time by choice. He looks well.

DISCUSSION OF CASES

Case 1 was known to have had essential hypertension since May 1943. It is probable that a psychologic factor precipitated the malignant phase of hypertension. His only treatment consisted of nephrectomy. He was returned to the same environment and for 22 months postoperatively has had a normal blood pressure.

Case 2 had almost the identical pathological changes as case 1. At the time of nephrectomy the dilated renal pelvis was empty of urine. This patient obtained no relief whatever from the hypertension.

It is of interest that autonomic blockade with TEAC caused little or no fall in blood pressure in case 1, whereas there was a marked depressor response in case 2 suggesting that a humoral mechanism was predominant in the former and a neurogenic mechanism in the latter. Whether or not the blood pressure response to autonomic blockade may be helpful in predicting the effect of nephrectomy in unilateral renal disease will, of course, require further study, but this does seem to be a suggestive lead.

In case 3, although the patient had been under the care of her private physician for a period of 2 years because of "high blood pressure," no records were kept of her blood pressure readings during this period. After admission to the hospital her blood pressure was recorded as 160/110. A hypertensive work-up was not done as it was thought that she had a urologic condition which required nephrectomy. Although the patient has a blood pressure of 130/70 three years after nephrectomy, proof of the presence of persistent hypertension before operation may be questioned.

In case 4 the patient was known to have normal blood pressure 3 years before admission. While under the observation of a competent observer, his blood pressure became rapidly elevated. Nephrectomy was not performed as it was thought the chances of improvement from this procedure seemed remote. After two more months on medical therapy he was readmitted in hypertensive crisis.

with a blood pressure of 210/120. A left nephrectomy was performed in "desperation"

This patient has been observed at frequent intervals for a 2 year period following operation. Besides his clinical improvement and reduction in albumin content of the urine, the most striking result has been in the diastolic blood pressure. The maximum diastolic blood pressure recorded has been 90 mm Hg.

DISCUSSION

On the basis of the evidence presented above it is evident that the relation of hypertension to chronic bilateral kidney disease is uncertain and that the urological surgeon has little to offer therapeutically. However, despite the experimental uncertainty of the role of unilateral kidney disease in producing hypertension, it is clear that removal of the unilaterally diseased kidney has improved or cured the hypertension in certain patients, although there is no method of predicting the results to be expected.

An important aspect of the problem is to develop methods of recognizing unilateral kidney disease when it occurs, and to differentiate between other "specific" types of hypertension such as pheochromocytoma.

In the final analysis the recognition of unilateral kidney disease depends upon a knowledge of the function of each kidney separately because in the absence of one functional kidney, the other can function well enough to produce normal results from routine renal function studies such as phenolsulfonphthalein and concentration dilution tests. It might be wise, therefore, to take excretory urograms as a routine diagnostic procedure in all cases of hypertension in order to recognize the presence of this condition where specific therapy can be offered to the patient.

Ferris and his group of investigators believe that testing the blood pressure response to TEAC is of value in recognizing those instances of hypertension where humoral factors predominate, for instance, the blood pressure in toxemia of pregnancy, in acute glomerulonephritis, and in pheochromocytoma, falls little or not at all during autonomic blockade, whereas in essential hypertension all gradations of response occur. It is of interest that the depressor response to TEAC in case 1 was very slight, which further supports the concept of a renal humoral mechanism in this case.

Pheochromocytoma is another unusual form of hypertension in which the urologist may offer specific treatment, and again the early recognition of this disease is of great importance.

Mention was made above of the lack of depressor response to autonomic blocking agents in the condition, in fact TEAC usually causes a pressor response.

The recent development of adrenolytic drugs, such as benzodioxane and dibenamine, has given us an important and specific test for the recognition of hypertension due to circulating adrenalin.²²

²² Shapiro, A. P., Harrison, M. B., Hoffman, M. S. and Ferris, E. B. *Am J Med*, 10 115, 1951.

²³ Goldenberg, M., Snyder, C. H., Aranow, H., *J.A.M.A.*, 135 971, 1947.

In pheochromocytoma the hypertension may be persistent, or it may occur in paroxysms. In the persistent form a consistent depressor response to benzo-dioxane is diagnostic of the disease. In the paroxysmal form, paroxysms of hypertension may occur spontaneously as the result of emotional stress and as the result of the administration of such agents as histamine, mechohyl, and TEAC. Since paroxysms of hypertension also occur frequently in essential hypertension it is important to test the specificity of the pressor response by abolishing it with benzo-dioxane. This then indicates that the pressor response was due to circulating adrenalin, and in this respect bolsters the diagnosis of pheochromocytoma.

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PERIPELVIC LIPOMA

SIDNEY IMMLRIGUT AND ZACHARY R. COTTLER

The medical literature contains reports of intrarenal, perirenal and parapelvic lipomas. The true lipomas, however, are extremely rare and must not be confused with replacement lipomatosis of the kidney proper and the parapelvic fibrolipomatosis commonly seen in cases of calculous disease with chronic infection. We present a case of true peripelvic lipoma involving the pelvis, calyces and proximal ureter. We have been unable to find a similar case in the recent literature.

CASE REPORT

I. G., a white woman 48 years old, consulted us on December 14, 1949 because of asymptomatic pyuria of 8 years' duration. She had a hysterectomy in 1941 and a routine urinalysis revealed the presence of pus cells. Although repeated examinations showed the constant presence of pus cells, a urological investigation never had been advised. Appendectomy and uterine fundectomy had been done 12 years ago. The patient had no urinary complaints.

Physical examination revealed a healed suprapubic midline scar. No abdominal masses or tenderness were found. Neither kidney was palpable. The blood pressure was 166/100, weight 140 pounds, temperature 98.6°F. Urine specific gravity 1.012, pH 6.5, albumin trace, glucose negative, sediment numerous white blood cells, singly and in clumps, occasional red blood cells.

A plain x-ray revealed a large calculus in the left renal area, overlying the twelfth rib (fig 1, A). Excretory urography demonstrated a normal right upper urinary tract. On the left side there was delayed excretion of the dye and marked dilatation of all the calyces. The calculus apparently occupied the pelvis of the kidney. There was no dye in the ureter. The lower pole of the kidney appeared to be displaced somewhat laterally.

Cystoscopy revealed a normal bladder. Both ureteral orifices were essentially normal. Indigo carmine appeared in 4 plus concentration from the right. There was no excretion of the dye from the left. A No. 5 ureteral catheter met an impassible obstruction at 24 cm. No urine was obtained by aspiration. A ureterogram revealed a marked narrowing of the upper ureter for approximately 4 cm below the distal tip of the calculus. The distal portion of the ureter was considerably dilated (fig 1, B).

It was our impression that we were dealing either with an intrinsic stricture of the ureter or a narrowing due to compression resulting from an old peri-ureteritis. The patient was hospitalized on January 3, 1950.

Laboratory data: Hemoglobin 97 per cent, erythrocytes 4,800,000, leukocytes 9,800 polymorphonuclears 66 per cent, lymphocytes 34 per cent, ESR 10 mm. Blood chemistry: Urea nitrogen 17.0 mg per cent, sugar 88 mg per cent, calcium 9.5 mg per cent, phosphorus 4.1 mg per cent, alkaline phosphatase 2.7 Bodansky units. The phenol-sulphonphthalein excretion was 46.8 per cent the first 60 minutes and 8.3 per cent the second 60 minutes. Urine culture was reported as showing *Staphylococcus albus*.



FIG. 1. A, plain X-ray demonstrating calculus in left renal area. B, retrograde study demonstrating marked narrowing of proximal ureter, ureteropelvic obstruction and dilatation of lower ureter.



FIG. 2. Splenic specimen. Note relationship of tumor to pelvis, calyces and ureter, as well as involvement of renal parenchyma.

Left nephrectomy with resection of the twelfth rib was performed on January 5, 1970, under hemispinal anesthesia. Convalescence was uneventful and the patient was discharged on the ninth postoperative day.

Pathological report: The left kidney measured 12 by 6 by 3 cm. and weighed 180 gm. Surrounding the pelvis and the attached 6 cm. of ureter was an en-

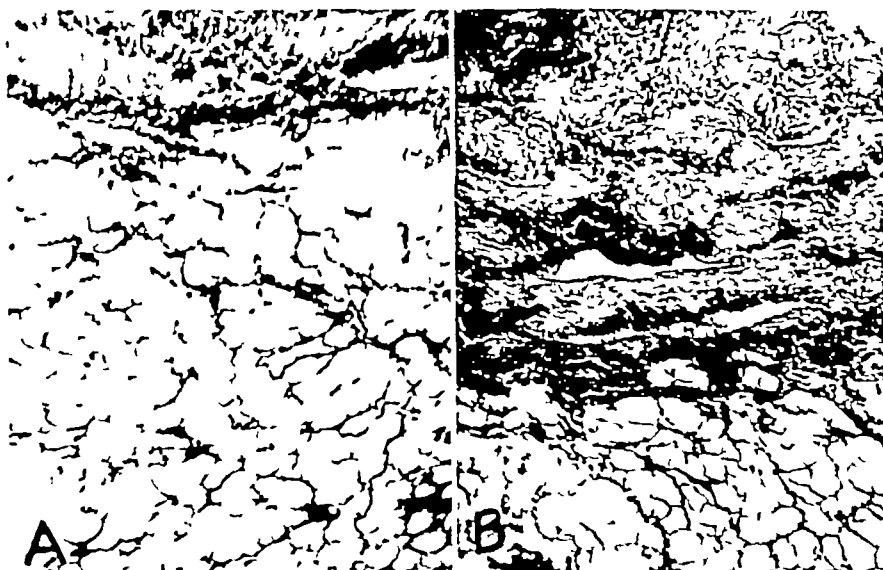


FIG 3 Demonstrating: A, typical microscopic appearance of lipoma; B, relationship to muscularis of pelvis ($\times 250$)



FIG 4 Area of ureteritis cystica ($\times 250$)

capsulated adipose tissue mass 8 by 4 by 4 cm. This adipose tissue was firmly adherent to the muscularis of the pelvis and ureter and appeared to arise from the adventitial coat. The lumen of the ureter coursing through the mass was markedly narrowed and barely admitted a fine probe. The external surface of

the kidney was red brown and the capsule stripped with ease revealing a granular scarred surface. On cut surface, the cortex and medulla were fully differentiated and measured 0.5 and 1.0 cm respectively. The cortex was tanned and the medulla grey-white and striated.

Upon opening the ureter, pelvis and calyces and splitting the kidney, the previously described adipose tissue was seen to completely surround these structures (fig. 2). Within the pelvis there was an irregular, grey-brown calculus 2 by 1 by 0.7 cm which projected into the lower calyx. The calyces were considerably dilated while the pelvis was not. The mucosa of the calyces was pinkish-grey, smooth and glistening while that of the pelvis was pinkish-grey and granular.

Microscopically the tumor was seen to be composed of typical adipose tissue cells and was derived from the adventitia. The muscularis was completely intact. One area of the ureter showed the presence of ureteritis cystica (figs. 3 and 4).
Diagnosis: Nephrolithiasis, pyelonephritis, hydronephrosis and peripelvic lipoma.

DISCUSSION

We have demonstrated grossly and histologically, a true case of peripelvic lipoma including the calyces and ureter. The inflammatory fibrolipomatosis commonly seen in cases associated with calculi and chronic infection can usually be dissected free from the pelvis once a line of cleavage has been established. This was impossible in our case because of the origin of the tumor within the true coat of the pelvis and its extension along the calyces and pelvis.

The constriction of the ureter and pelvis due to the lipoma with its attendant stasis and back pressure effects most probably led to the formation of the calculus found here.

The diagnosis of a true peripelvic lipoma can only be made at the time of operation. Preoperatively, as illustrated by the retrograde study (fig. 2), one would be more justified to make a diagnosis of stricture, and if a calculus and pyuria are present to consider it inflammatory.

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SQUAMOUS CELL CARCINOMA OF THE RENAL PELVIS

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The incidence of squamous cell carcinoma of the renal pelvis is low, with some 81 cases having been reported in the literature. Of these, 5 cases have been in kidneys with congenital anomalies and/or in ptosed kidneys. The case presented is an occurrence in a ptosed kidney of long standing.

Another and frequent occurrence is the simultaneous finding of infection and/or calculus formation in the same kidney with the squamous cell carcinoma of the renal pelvis. Melicow says that infection and stone formation are so frequent that they are to be considered in the symptom complex of this entity. A suggestion as to etiology of this tumor can be made. Stone and/or infection superimposed on a normally or ectopically placed kidney leads to metaplasia of transitional to squamous epithelium, which undergoes metaplasia to leukoplakia, which in turn develops into squamous cell carcinoma. Kutzmann says that leukoplakia and squamous cell carcinoma of the renal pelvis co-existed in 11.9 per cent of 67 cases.

CASE REPORT

F. B. GRIMM A-182456, an 80-year-old white woman, was admitted to Grady Memorial Hospital on July 17, 1949 with a complaint of recurrent episodes of painless hematuria for 2 months. She admitted having two or three short episodes of frequency and dysuria before the hematuria began. (The veracity of her history was questionable due to her desire to entertain all who questioned or examined her.)

Physical examination revealed a thin, elderly woman, quite alert, but pale, and not appearing acutely ill.

The positive physical findings were limited to her abdomen. No organs or tenderness elicited. The lower abdomen and pelvis were filled with a nontender, movable mass about the size of a 5-months gravid uterus.

On further questioning the patient stated that the mass had never been painful and that it had been appearing and disappearing at long intervals since her last pregnancy 55 years ago.

Laboratory studies: Urine pH 6.5, specific gravity 1.015, albumin 3+, microscopic study showed innumerable red blood cells per high power field, urine culture: *E. coli* on two specimens. Red blood cells 2,950,000, hemoglobin 9.5 gm., white blood cells 11,000 with normal differential, nonprotein nitrogen 31. Electrocardiogram showed changes compatible with age.

Cystoscopy showed that the bladder was moderately inflamed throughout. A diverticulum was seen on the right wall near the right ureteral orifice. Blood was seen to come from the right ureteral orifice and clear urine from the left. An obstruction was met at 20 cm. up the right ureter and 30 cc. of bloody urine was withdrawn. Retrograde pyelograms were made (fig. 1).

To prepare the patient for surgery two whole blood transfusions were given. Following the second transfusion she had chills, fever and was quite ill. She recovered under conservative treatment. Since the mass appeared smaller and caused no symptoms the patient was discharged on July 28, 1949.

She was readmitted on August 5, 1949. The abdominal mass was now painful and she appeared to be quite ill. Physical and laboratory findings were similar to those at the previous admission except for the abdominal mass which had noticeably increased in size. With the patient lying flat it protruded about 3 inches above the level of the abdominal wall. Pelvic pressure by the mass caused her to void every 20 to 30 minutes. It was apparent that surgery was now a



FIG. 1. Pelvic mass showing protruding kidney and tremendously dilated pelvis forming a tumor.

necessity. She was given 1500 cc whole blood by transfusion without reaction. During her preoperative period the mass enlarged daily.

The preoperative diagnosis was hydronephrosis in a congenital ectopic kidney. Tumor was considered a possibility and a search for metastases was negative. On August 13, 1949, a transperitoneal nephrectomy was done under spinal anesthesia and pentothal analgesia through a right rectus incision without incident. The pelvis of the kidney was found to be in a normal position, therefore the kidney was placed inside of ectopic. No local metastases were found. She had a smooth postoperative course and was discharged symptom-free and completely ambulatory on the fifteenth postoperative day.

When seen at the Center 12, 1949, the patient was well, she had gained about 10 pounds since her operation and was conducting light housekeeping duties.

Postoperative weight 11000 gm. at days 2 and 5. The pelvis was thin-walled and

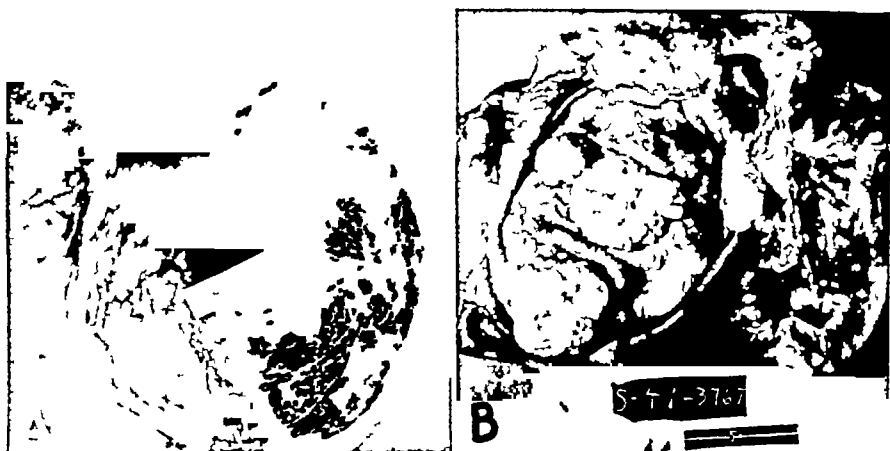


FIG 2 A, kidney specimen showing greatly enlarged pelvis which was filled with 1000 cc purulent material B specimen with pelvis and kidney cut open showing multiple tumor growths in pelvis



FIG 3 A same as figure 2 B B close up view of one of larger tumors of pelvis showing tumor cut open



FIG. 1. A: low-power view of polypoid epithelium that has undergone squamous metaplasia. B: high-power view of the same area.

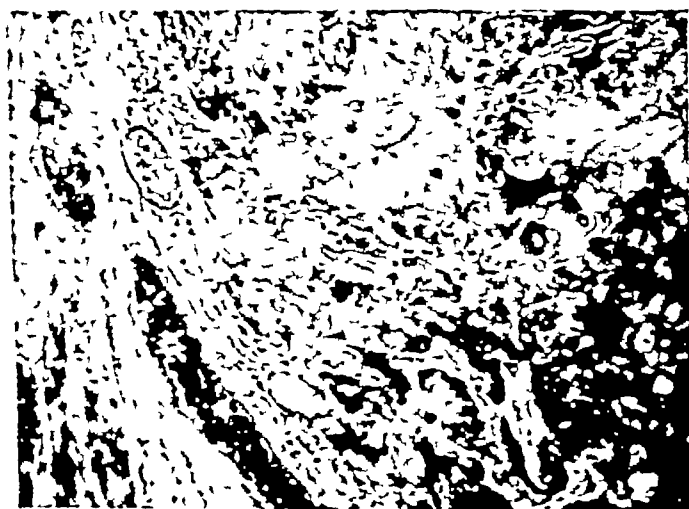


FIG. 2. Section stained with hematoxylin and eosin. Two keratin cysts of tumor. Notice hyperchromatic nuclei.



FIG. 6. A, section of kidney showing acute and chronic pyelonephritis. B, section of renal pelvis showing squamous metaplasia.

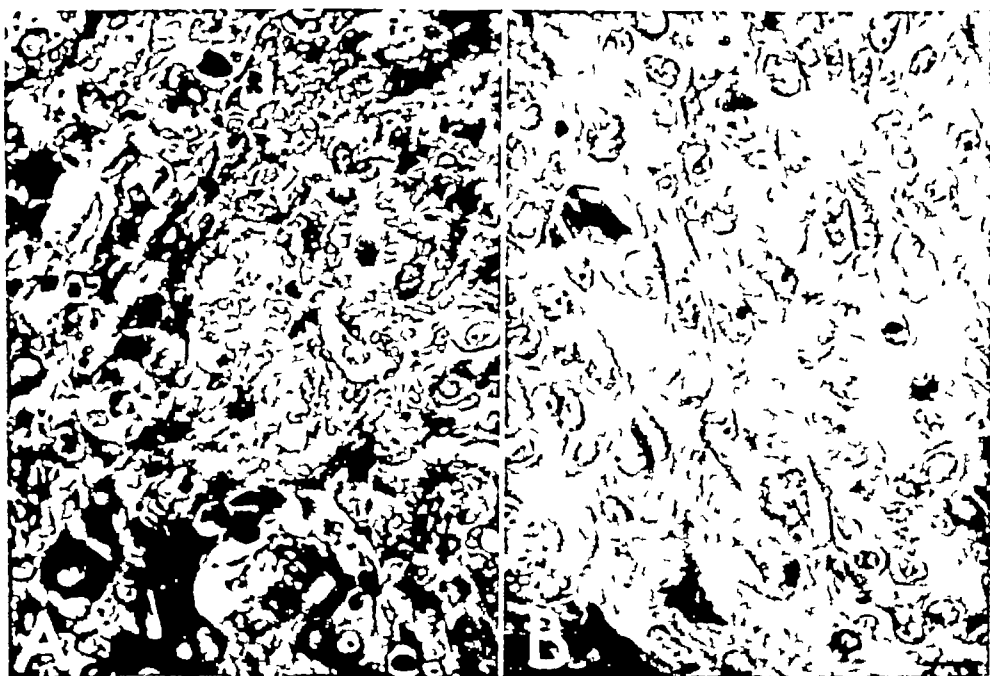


FIG. 7. A, high power view of squamous cell carcinoma. B, section of pelvic epithelium showing leukoplakia.

multiple tumor masses could be palpated through the wall of the pelvis. When the pelvis was opened, 1000 cc of foul-smelling purulent material escaped. The pelvis showed in addition to the tumors illustrated, several areas of somewhat wrinkled leukoplakia, rather sharply circumscribed, which measured from 4 mm to 2.5 cm in circumference and were raised 2 to 4 mm from the pelvic mucosal surface. The tumor noted at the ureteropelvic junction probably acted as a ball-valve and thus produced the hydronephrosis.

Microscopic study of the sections showed squamous cell carcinoma of the renal pelvis, multicentric squamous metaplasia of the renal pelvis, leukoplakia, and marked acute and chronic pyelonephritis (figs 4, 5, 6, and 7).

The patient died in a nursing home in July 1950. An autopsy was refused. The last follow-up in June 1950, showed no evidence of return of the squamous cell carcinoma. Complete x-ray studies and a physical examination were made in an attempt to find evidence of metastasis but were negative.

SUMMARY AND CONCLUSIONS

The case presented here presents a rare end result to longstanding renal infection. It emphasizes the relative high frequency of squamous cell carcinoma of the renal pelvis with associated obstruction and anomalies of formation and position.

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BIOPSY OF THE KIDNEY FOR SUSPECTED NEOPLASM

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Although conservatism is a prime consideration in renal surgery, many kidneys have been sacrificed needlessly because of suspected neoplasm. When exposure of the kidney reveals an obviously benign lesion, such as a cyst, removal of the cyst is the accepted procedure. However, in cases in which the findings suggest the possibility of tumor, if a benign lesion is not evident upon external inspection, nephrectomy has been considered mandatory. A possible alternative, incision into the kidney for diagnostic purposes, has been condemned, since it is alleged that 1) there is danger of disseminating tumor cells if a malignancy is present (fig. 1), and 2) a small tumor may escape detection.

With refinements in technical diagnostic procedures the need for exploratory operation in all types of surgery has progressively diminished. More accurate information can usually be obtained about the kidney by cystoscopic and roentgenographical studies than by exposure of the organ at operation. Yet in some cases, not infrequent in urologic practice, it is impossible to differentiate between a benign and malignant lesion without incision into the kidney.

In an attempt to preserve the kidneys of those patients with benign lesions, we undertook development of a safe technique of renal biopsy. We shall show that in selected cases such a procedure can be performed without additional risk to patients with early tumor. Furthermore, we believe that when it is demonstrated that operation can be performed without needlessly sacrificing a kidney, patients with suspected renal tumor will come to earlier operation.

It is interesting to speculate why biopsy of some urogenital organs is considered safe while biopsy of others is considered hazardous. There is no hesitancy, for example, in excising tissue from the bladder or penis and waiting for an unhurried pathological examination before proceeding with treatment. In suspected carcinoma of the prostate, some urologists perform punch biopsy and others massage the gland to obtain secretion for examination by Papanicolaou's technique. Yet biopsy of the kidney and testis has been generally condemned, even if immediately followed by radical operation.

In explaining the rationale of such apparently conflicting policies, it may be maintained perhaps that cells of tumors of low grade malignancy are less subject to dissemination than those of highly malignant tumors undergoing rapid proliferation. It is also possible that the hazard may be greater in an extremely vascular organ as the kidney.

Read at meeting of Urologic Section, New York Academy of Medicine, January 18, 1950.

Reviewed in the Veterans' Administration and published with the approval of the chief medical director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans' Administration.

It is recognized that most renal tumors are highly malignant and that the organ has an abundant blood supply. However 1) if the kidney can be temporarily isolated and if necessary removed subsequently without danger of disseminating tumor cells and 2) if the error of failing to discover an early malignant tumor is avoided by proper selection of cases, renal biopsy should be recognized as a safe procedure.

We shall first review the literature on biopsy, gleanings therefrom relevant information from previous investigators. Secondly, we shall present experimental data regarding the safety of a method we have developed for renal biopsy, and, finally, we shall demonstrate the clinical application of the method with illustrative cases.

Alleged Dangers of Biopsy

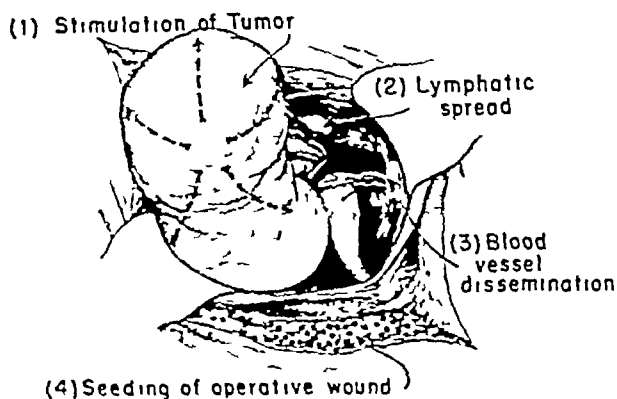


FIG. 1

A REVIEW OF BIOPSY

During the middle of the nineteenth century ideas about biopsy were first expressed in various independent reports. It was Virchow, however, who in 1854 made the first clinical application. Since then, of a number of experimental studies and clinical reports, assuring the hazards of biopsy, a few stand out.

In experiments in which rats were inoculated with Flexner-Jobling carcinoma, no more metastatic lesions developed in a group that underwent partial excision 10 to 12 days prior to complete excision than in another group in which complete excision was performed immediately (table 1). The conclusion reached was that cutting into a tumor prior to its excision does not disseminate tumor cells.

Further light was shed by an interesting experimental study of dangers in the use of local infiltration anesthesia in operations on malignant tumors (table 2). After excision of tumors in mice, the incidence of pulmonary metastasis was higher in animals that underwent infiltration of a local anesthetic agent in and about the tumor than in others given a general anesthetic. On the basis of these results it was concluded that local infiltration anesthesia for biopsy or removal of malignant tumors is dangerous and should be avoided.

The effect of biopsy and partial excision of various types of experimental tumors in rats has been investigated (table 3). Simple biopsy of adenocarcinoma

and squamous cell carcinoma did not affect the survival period or the incidence of pulmonary and lymph node metastasis

TABLE 1 *Result of delay between partial and complete excision of Fleischer-Johling rat carcinoma in 673 white rats*

All animals were sacrificed 3 to 4 weeks after inoculation with carcinoma cells

GROUP	PROCEDURE	PER CENT WITH METASTASIS TO LUNG AND REGIONAL LYMPH NODES
1	Delay of 12-14 days between partial and complete excision of tumor	22.2
2	Complete excision of tumor	21.8
3	Controls	32.2

Wood, 1919

TABLE 2 *Effect of injection of 1 cc of 0.5% novocaine prior to removal of tumor. In controls tumor removed under general anaesthesia*

TUMOR	NUMBER MICE		NUMBER WITH PULMONARY METASTASES		P
	Control	Experimental	Control	Experimental	
Sarcoma	50	50	0	2	0.162
Adenocarcinoma	46	46	9	15	0.273
Tumor G	48	58	5	20	0.020
Tumor D	40	42	4	13	0.058

Peyton 1940

* P—The factor of probability

TABLE 3 *Transplanted tumors in rats: period of survival and percentage of metastases*

TYPE OF TUMOR	PROCEDURE	NO. RATS	GROUP	DAYS SURVIVED	METASTASES	
					Lymph node	Lung
Fibrosarcoma	Almost total excision	19	Control	28	79%	90%
		19	Excised	42	63%	84%
Adenocarcinoma breast	Partial excision	19	Control	98	5%	26%
		20	Excised	125	15%	60%
Adenocarcinoma breast	Simple biopsy	20	Control	110		20%
		18	Biopsy	114		22%
Squamous cell carcinoma	Simple biopsy	31	Control	93	97%	91%
		20	Biopsy	95	100%	90%

Mann and Dunning 1946

In a carefully controlled clinical study, the effects of biopsy were observed in 166 selected cases of squamous cell carcinoma of the mouth, lip and penis (table 1). In approximately half of the cases biopsy was performed without any attempt to minimize the associated trauma. The control group consisted of cases in which a clinical diagnosis was made without biopsy. All were treated similarly and

follow-up for 2 years showed that the incidence of metastasis in the patients who had undergone biopsy was not higher.

Experimental workers early discovered a factor apart from biopsy, which ranks high in the production of metastasis. It was found that massage forced showers of tumor cell emboli into the blood stream and lymphatics producing a greatly increased incidence of metastasis.

In Japanese waltzing mice inoculated with carcinoma, incidence of visceral metastasis was higher in mice in which massage was given than in the controls.

TABLE 4 Incidence of metastases in 166 cases of squamous carcinoma 2 year follow up

CASES	REGIONAL NODES INVOLVED	DISTANT METASTASES	ALL METASTASES
Biopsy 99	16 (15%)	3 (2%)	19 (19%)
No biopsy 67	13 (19%)	1 (1.5%)	14 (20.5%)

Paterson and Nuttal 1939

TABLE 5 Incidence of visceral metastases in mice following massage of inoculated carcinoma

Experiment 5

Massage on 27 29 33 34 35 days, killed 45 days

	METASTASES
Experimental 11 mice	7 (63.3%)
Controls 11	3 (27%)

Experiment 6

Massage on 18 21 days killed 36 days

	METASTASES
Experimental 10 mice	8 (80%)
Controls 10	0

Tazzer 1913

TABLE 6 Force required to separate pairs of cells by micromanipulation

Normal Hip	1.42 mg
Carcinoma Hip	0.47
Normal Cervix	1.25 mg
Carcinoma Cervix	0.18

Coman 1946

Factors influencing experimental metastasis

Table 5. It was concluded that in artificially produced tumors metastasis is enhanced by manipulation and this is accomplished as readily during the early development of a tumor as during the period in which metastasis naturally occurs.

In all other experimental studies with a micromanipulator a lack of cohesive tumor cells was observed (table 6). Such a factor would increase the possibility of tumor cells being released during manipulation of a tumor. As a result of this a large percentage of spontaneous mammary tumors in 50 mice

produced a 22 per cent increase in macroscopically discernible metastases (Marsh) The implication was that manipulation is dangerous in human cancer

In no series of clinical cases have the dangers of manipulation been proved, but deductions have been drawn on the basis of clinical impressions and isolated case reports W J Mayo advised treating a tumor as one would a focus of virulent infection, because of the danger of inducing metastasis Knox reported that extensive metastasis was frequently noted after osteopathic treatment of malignant tumors, citing an instance of a breast tumor with widespread invasion of the pectoralis muscle Surgeons have advised against manipulation and diagnostic curettage of the uterus when the possibility of cancer is present because of the hazard of releasing fragments into the blood stream or peritoneal cavity (Simpson) A case of extensive dissemination of a breast carcinoma, apparently spread by dily application of an ointment over a period of three years, has been reported (Dial) Bambridge attributes his excellent end results in the treatment of breast cancer to the avoidance of trauma during radical mastectomy

Obviously, sweeping conclusions concerning the hazards of biopsy cannot be drawn from perusal of the literature It is not only impractical to run adequately controlled series in human beings, but also the action of different types of tumors and the individual response in both animals and humans varies greatly However, the reports indicate that incision into a tumor is a relatively innocuous procedure, whereas a more potent source of danger is manipulation, whether prior to or during operation

THE DANGERS OF RENAL BIOPSY

Although the possible danger of spreading tumor cells during operative exposure of the kidney may be minimized by certain steps to be outlined, there is no way of entirely avoiding this hazard, since exposure is as necessary for nephrectomy as for biopsy However, since renal tumors are so notably malignant, and since the organ has such profuse vascular and lymphatic connections, it seemed necessary to develop a technique of incising the kidney which would present no more risk of disseminating tumor cells than nephrectomy

This problem was facilitated by the fact that the anatomical structure of the kidney is well adapted for biopsy At operation the kidney can be easily isolated, leaving attachments only at the vascular pedicle and ureter, structures which lend themselves to periods of temporary occlusion In 1949, Scheibe, Giraldi and Vermeulen showed that the period of safety during which the vascular pedicle may be completely compressed is much longer than it was previously believed to be In determining the effect of temporary occlusion of the renal vein and of the entire pedicle dogs and rats from which one kidney had been removed were used The amount of renal damage was estimated after varied periods of compression by determining the level of the blood urea nitrogen and by studying the microscopic changes in the kidneys The renal vein in the rat was occluded for 30 minutes and the entire pedicle for 90 minutes and for twice these periods in the dog without significant renal damage (table 7) These findings are in accord with our clinical observations following nephrotomy We have found that the

safety period for occlusion of the vascular pedicle is more than adequate to permit the most painstaking biopsy including time for frozen section if necessary.

In our experimental studies the release of tumor cells was simulated by injecting tracer substances into the renal parenchyma following isolation of the kidney and compression of the vascular pedicle and ureter. Since injection into the kidney is made under pressure, whereas there is release of pressure during incision of a tumor, this test seemed more than fair evaluation. Following injection of the tracer material the kidney was removed and samples of tissue taken from various parts of the animal were examined for the presence of the injected substance.

TABLE 7 *Danger period for occlusion of renal vessels*

	RAT	DOG
Pedal vein	30 min	60 min
Entire pedicle	90 min	150 min

Schiebe, Giraldu and Vermeulen 1949

RELATIVE SIZE OF TRACER SUBSTANCES

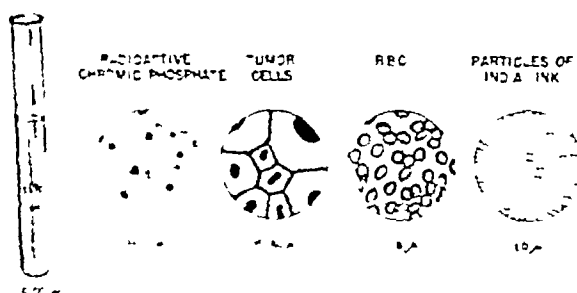


FIG. 2

PRELIMINARY TESTS

In preliminary tests several tracer substances and methods were evaluated. In using rats, guinea pigs and dogs, the latter animals were the ones chosen for the final tests because their larger size made them the most satisfactory.

Indiank was the first material used as a tracer medium, but this was unsatisfactory for identifying small numbers of particles. In our search for a suitable tracer, radioactive isotopes were found to be better suited for our purpose, since their presence can be detected in the most infinitesimal amounts, approximately 1 part in 10 million. In early studies P^{32} in a solution of disodium phosphate was used. Radioactive ions in solution, however, diffused through body tissue, and this diffusion did not simulate dissemination of tumor cells. Studies were therefore continued with radioactive chromium phosphate, a colloidal preparation composed of radioactive particles smaller than tumor cell emboli. The colloidal particles ranged from 0.1 to 5.0 microns in diameter, tumor cells average 15 to 60 microns in diameter (fig. 2). This medium proved to be ideal.

EXPERIMENTAL METHOD IN DOG

Preparation of radio-active materials The P^{32} was administered either as disodium phosphate in isotonic saline or as chromic phosphate prepared according to the method of Jones, Wrobel and Lyons. The concentration of disodium phosphate solution was 75 to 187 microcuries per cc, whereas the concentration of chromic phosphate, a colloidal suspension of much greater radioactive concentration ranged from 375 to 1500 microcuries per cc. The greater radioactivity of the latter preparation becomes apparent when the calculated dose from assay of the injected kidneys is noted (tables 11 and 12).

Operative technique Dogs weighing 5.5 to 14.0 kg. were anesthetized intravenously with 28 mg. per kilogram of sodium pentobarbital, and the kidney exposed through a lumbar incision. The ureter was freed well below the renal pelvis and the vascular pedicle was isolated, care being taken that no other tissues remained as a bridge. In all instances the ureter was occluded with a rubber-tipped clamp. The vascular pedicle was also compressed, either with a rubber-tipped

Experimental Method

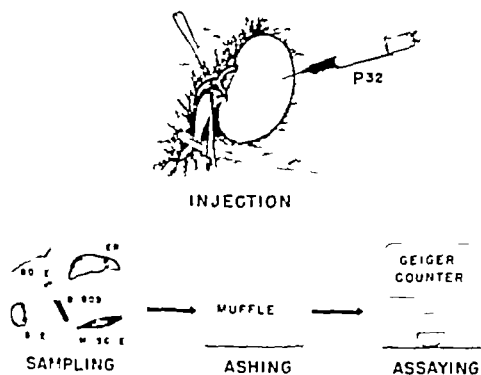


FIG. 3. Method of injection of radio-active tracer substances into parenchyma of isolated kidney in dog. Kidney removed after 0 minutes and samples assayed for radioactivity to determine possible dissemination.

clamp or with a rubber tourniquet. Although either method was satisfactory in the dog, it was more convenient to apply a clamp for the 30 minute period of the experiment than to use the tourniquet. The operative wound was protected from contamination by laparotomy tapes. One cubic centimeter of tracer material was thereupon injected into the renal parenchyma with a 26 gauge needle, care being taken to avoid penetration of the renal pelvis (fig. 3).

Complete compression of the pedicle and ureter was maintained for 30 minutes and during this time the kidney was manipulated as it is during biopsy. After this period the organ was amputated by the use of clamps without releasing tension on the pedicle or ureter. The animal was sacrificed by bilateral pneumothorax and representative samples taken for assay.

METHOD OF SAMPLING AND ASSAY

In addition to the kidney, samples of blood, liver, muscle and bone were examined. Each weighed at least 30 gm. Prior to radioactive assay, all samples were

ashed in an electric muffle at 550°C. The entire ash from all of the tissues except bone was assayed for radio phosphorus. In the case of bone, a composite sample of 5 gm. was selected from the femur. The samples were placed in porcelain dishes for radioactive assay. Corrections were made for self absorption due to the mass of the sample.

A thin-window, bell-shaped Geiger Müller counter was used for radioactive assay, the results are expressed in counts per second. The time elapsed for 1 024 counts was measured. The statistical fluctuation for this number of counts is less than plus or minus 5 per cent. The total counts measured arose from 1) the background of the instrument, 2) the initial radioactivity of the sample due to naturally occurring K^{40} as well as other chance contamination not related to P^{32} , and 3) activity arising from the sample itself from P^{32} administered. The background of the tube under the conditions used varied from 1 to 1.3 counts per second.

TABLE 8. Sample calculation—*injection of chromic phosphate*

(1.5 MC diluted to 40 cc)

(Dose = 10 cc or 3.5 microcurie/dog)

T TIAL WET WEIGHT	TOTAL ASH WEIGHT	ACTUAL MEASUREMENT		MASS ABSORP TION CORREC TION	CORRECTED c/s FOR MASS ABSORPTION	% OF DOSE PER GRAM WET WEIGHT	
		Counts/Second	Corrected c/s				
Dog No. 2—kidney clamped off. Injected 3/3/49 received 3.349							
1	0.0 cc	0.25 gm	1094.76	0.10c/s	94	0.11c/s	0.0000001%
1	17.0 gr	0.7 gm	1094.391	1.77c/s	83	2.14c/s	0.0000019%
1	2.0 cc	0.7 gm	1094.14	$\times 3.3 = 2.903.25c$	62	$3.155.71 \times 1000 = 3.155.710c/s$	
1	4.0 cc	0.7 gm	1014.4	0.67c	57	0.77c	0.0000005%
1	1.0 cc	0.7 gm	1014.4	0.12c	45	$0.27 \times 2.50 = 0.67c$ Total = 0.70c/s	0.0000007%

All kidney measurements were made on 3/3/49 and all results are related to the Tracerlab Autoscaler Shell 5 by a factor of 1.17.

The geometry of the measuring instrument was such that one microcurie produced 6000 counts per second. Table 8 shows how the calculations were made.

RESULTS OF EXPERIMENTS

Animal tissues contain a small amount of radio activity which results from naturally occurring K^{40} and chance contamination other than P^{32} . The natural radio activity in the tissues of 10 experimental animals was therefore determined to serve as control readings and aid in the interpretation of the results after injection (table 9). It will be seen that under natural conditions blood, liver, muscle and bone may have radio activity of up to 4.6 counts per second.

Numerous control readings were made (table 10). The effect of injecting 1 cc. radioactive disodium phosphate into the kidney without compression of the pedicle or ureter was tested. Appreciable amounts of the tracer substance were detected in all of the tissue sampled. Under similar conditions, after injection

of 1 cc radio active phosphate it was found in all tissues tested. In one animal in which the vascular pedicle but not the ureter was compressed, there was slight detectable radio activity only in the liver, possibly indicating spread through

TABLE 9. *Natural radioactivity in dogs*

Animal tissues contain a small amount of radioactivity resulting from naturally occurring K^4 and chance contamination other than P^{32}

Dog	COUNTS PER SECOND			
	Blood	Liver	Muscle	Bone
15	0.1	2.1	1.7	0.0
16	0.4	4.6	1.1	0.0
19	0.2	0.2	0.5	0.1
20	0.4	0.4	0.1	0.1
21	0.0	0.3	0.4	0.0
22	0.0	0.6	0.1	0.0
23	0.1	3.8	0.5	0.0
24	0.2	1.1	0.6	0.0
31	1.3	—	1.8	—
32	1.2	—	1.7	—

TABLE 10. *Controls. Solution of disodium phosphate containing P^{32} injected*

Control experiments demonstrate leakage of radioactive tracer in absence of complete renal isolation. There is more dissemination through vascular pedicle than ureter. Even momentary release of pedicle clamp results in leakage.

Without compression of pedicle

Dog	DEFINITE TOTAL COUNTS PER SECOND	COUNTS PER SECOND				PROXIMAL PEDICLE
		Blood	Liver	Muscle	Bone	
13	7,100.0	56.3	106.6	43.3	36.6	
14	700.321.1	12,741.8	48,416.5	40,001.2	23,653.7	

Radioactive colloidal chromic phosphate injected

Without compression of pedicle

15	2,200.000	10.3	1060.0	770.0	390.0	19,400.0
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Without compression of ureter (pedicle occluded)

16	2,200.000	0.5	9.7	0.6	0.0	2.5
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Pedicle clamp momentarily released before nephrectomy

17	923.130.0	—	12.5	172.5	172.9	
18	2,104.330.0	127.3	0.8	2.5	0.4	

the lymphatics by way of the portal system. In 2 dogs the effect of momentary release of the vascular pedicle prior to nephrectomy was tested. After injection of radio active chromic phosphate with compression of the pedicle and ureter for 50 minutes the vascular pedicle was momentarily released before re-applying

the clamps for removing the kidney. In one animal the radio-active material was immediately apparent in the blood but in none of the other tissues tested in the other animal small amounts were detected in all samples.

Series 1 twelve dogs: injection of soluble radio-active disodium phosphate into the kidney under experimental conditions. Although less radio-active material was detected in the samples than in the controls, the compressed pedicle and ureter were penetrated by the tracer material (table 11). In view of subsequent results with a colloidal suspension, we believe this penetration is entirely attributable to the diffusible nature of disodium phosphate, which existed in solution in ionic form.

Series 2 twelve dogs: injection of radio-active chromic phosphate, a colloidal suspension into the kidney under experimental conditions. In this series (table 12) the radio activity of the samples tested is all accounted for by natural sources.

TABLE 11. Solution of disodium phosphate containing P^{32}

Use of diffusible radioactive solution resulted in occasional minimal leakage. Subsequent experiments with particulate isotopes showed no dissemination (table 12).

S	TOTAL COUNTS PER FOOT OF 1 INCH OF KIDNEY	COUNTS PER SECOND			
		Blood	Liver	Muscle	Bone
1	649,000.0	0.2	0.9	1.3	0.0
2	2,323,323.0	56.2	59.8	40.9	113.9
3	201,390.0	21.5	98.7	15.3	15.6
4	239,690.0	1.4	3.4	1.9	1.1
5	260,160.0	2.5	5.8	1.7	2.2
6	290,150.0	5.4	5.5	3.4	3.2
7	589,735.0	5.5	15.8	10.4	0.3
8	597,329.0	0.1	2.1	14.1	0.7
9	594,721.0	8.3	18.5	9.7	12.2
10	489,020.0	68.0	132.0	69.3	151.4
11	219,090.0	3.2	9.2	3.8	2.1
12	292,090.0	1.9	1.1	1.6	0.2

for which no correction was made. There is no evidence that the pedicle or ureter was penetrated by any of the radio-active particles. In addition to the usual samples tested, a block section of the tissues incorporating the proximal portion of the vascular pedicle, the ureter distal to the point of division and the surrounding tissue was assayed for radio activity in 6 dogs of this series. No evidence of penetration into this adjacent area was found.

It seems justifiable to conclude on the basis of these experiments that the kidney may be incised safely without danger of spreading tumor cells. As regards the technique described, the possible danger of momentary release of the vascular pedicle prior to nephrectomy is demonstrated. If a malignant lesion is found the way of greatest safety lies in applying pedicle clamps distal to the point of compression without release of tension during their application. Since the experimental method may be more exacting than that required clinically, and since there is no evidence that tumor emboli frequently occur without the develop-

ment of metastases this may be an unnecessary precaution, yet any error in adhering to this technique is in the direction of added safety. Compression of the ureter may be a superfluous step, since tumors of the parenchyma do not spread down the ureter. However, it is possible that the intercommunication between the blood vessels and lymphatics of the kidney and the upper portion of the ureter provide a channel for escape of tumor cells, and that this step likewise adds to the safety of the procedure.

CLINICAL APPLICATION

The successful use of renal biopsy depends upon the careful selection of cases. It is indicated only in those patients with pyelographic findings suggestive of a small, localized, space-consuming lesion of the parenchyma.

TABLE 12 *Radioactive colloidal chromic phosphate*

Injection of colloidal chromic phosphate with radioactive particles smaller than tumor cells produced no dissemination. Counts up to 3 per second may be attributed to background and natural radioactivity of tissues.

No.	DOSE IN TOTAL COUNTS PER SECOND INJECTED KIDNEY	RADIOACTIVITY IN COUNTS PER SECOND								
		Pre injection				Post injection				
		Blood	Liver	Muscle	Bone	Blood	Liver	Muscle	Bone	Proximal Pedicle
19	3 600 000	0.2	0.2	0.5	0.1	0.0	0.3	0.8	0.1	0.0
20	3 600 000	0.4	0.4	0.1	0.1	0.0	0.6	0.7	0.0	0.1
21	3 600 000	0.0	0.3	0.4	0.0	0.3	0.5	1.3	0.0	0.3
22	3 600 000	0.0	0.6	0.1	0.0	0.0	1.0	0.7	0.1	0.1
23	2 200 000	0.1	3.8	0.5	0.0	0.4	2.4	0.5	0.9	2.3
24	2 200 000	0.2	1.1	0.6	0.0	2.0	1.3	0.5	0.1	0.3
25	3 155 710					0.1	2.1	0.8	0.7	
26	1 591 530					0.1	0.8	3.1	3.0	
27	1 800 000					0.0	0.5	0.6	0.0	
28	9 600 000					0.0	0.2	0.6	0.0	
29	7 800 000					1.5	1.7	1.9	1.0	
30	6 500 000					1.0	1.5	1.7	1.0	

Biopsy is not indicated when 1) the diagnosis of malignant tumor has been established as by the Papanicolaou technique, 2) when a kidney is functionless, and 3) in large neoplasms which are obvious on external inspection. Nor is biopsy adapted to 4) those patients who suffer from obscure unexplained bleeding from one kidney when the pyelogram yields no clue to the nature or location of the lesion. In these latter cases, if operation becomes necessary, nephrectomy should be performed. Bisecting the kidney in a blind endeavor to determine the source of obscure bleeding is practically always fruitless.

In the application of renal biopsy it is pertinent to consider the various abnormalities which may produce pyelographic changes indicative of a space-consuming lesion within the parenchyma. Tumors of the renal pelvis present a different clinical problem and are not of concern in the present discussion. The various abnormalities which either constitute or simulate a space-consuming lesion of the parenchyma are:

1. *Neoplasms*. It has been observed that renal tumors may arise from any point in the parenchyma (Cahill). Although most of these tumors are malignant, they are usually surrounded by a definite fibrous capsule during their early growth. This characteristic is intimately concerned with the problem of biopsy and surgical treatment. Examination of operative specimens shows that involvement of the perinephric fat is by direct growth and that prior to such extension there is a latent period when the tumor remains confined by the fibrous capsule. Penetration of the capsule is a late phenomenon and does not usually occur in small tumors which might be encountered upon biopsy.

Vermooten is so impressed with the localization of early malignancies that he recommends local excision of the tumor whenever the opposite kidney is functionally inadequate. He believes that such a procedure is sometimes justifiable when the opposite kidney is normal. His judgment is based upon a comprehensive pathological survey including personal examination of 30 operative specimens of clear cell carcinoma. With rare exception, the tumors he studied were confined within a fibrous capsule and none had invaded the perinephrium.

Bell correlated the size of 153 malignant renal tumors with their metastases. Of those under 5 cm. in diameter only 7 per cent had metastasized whereas 83

TABLE 13. Size of 129 adenocarcinomas correlated with incidence of metastases (necropsy findings)

SIZE OF TUMOR	TOTAL CASES	METASTASES		NO METASTASES	
		Cases	Per cent	Cases	Per cent
Under 5 cm.	65	5	7.7	60	92.3
Over 5 cm.	84	69	78.6	8	21.4

Bell, 1938

per cent of those over 5 cm. in diameter had metastasized (table 13). This observation indicates that although the size of the tumor is not a certain criterion, the larger tumors are more likely to metastasize.

2. *Cysts*. Cysts of the kidney may be of any size, either single, multiple, or multiloculated. They may develop at any point within the parenchyma.

3. *Infection*. An abscess or carbuncle of the kidney may likewise be located anywhere in the parenchyma. Circumization incident to chronic pyelonephritis may produce a deformity that resembles a space-consuming lesion.

4. *Arteriole*. Malformations of the renal pelvis frequently simulate a space-consuming lesion of the parenchyma. An appearance of spreading apart of the calyces may be produced by blind kidneys; less commonly, as the result of malrotation, which usually yields the picture of diffuse deformity. Malformation of one calyx may give the pyelographic picture of compression or elongation. This appearance may also be produced by peripelvic fat accumulation.

5. *Trauma*. Following injury the presence of blood or the development of scars may produce a deformity suggestive of a mass within the kidney.

6. *Calcification*. It is often impossible to differentiate between the benign and malignant lesions. Various symptoms and signs may be helpful, yet none are pathognomonic. The history may suggest a traumatic lesion; a febrile course may

indicate carbuncle or abscess, but the differentiation between early tumor, cyst or nodulous formation of the renal pelvis may present tremendous diagnostic difficulty. While bleeding from the kidney is more suggestive of renal tumor, it also occurs in approximately 10 per cent of serous cysts. Although a perfectly round pyelographic filling defect may suggest a cyst, the identical findings may be produced by early neoplasm. An elongated cephalic calyx may suggest renal neoplasm as well as nodulous formation of the pelvis.

The grave prognosis which attends malignant tumors of the kidney is due to their proverbial silence in the early stage; many are undetected until all hope for cure has passed. In the early, curable stage they are occasionally discovered 1) during a search for the cause of gross hematuria, 2) in the course of an investigation of the cause of microscopic hematuria found on routine examination of the urine, or 3) when suspicious filling defects are seen in pyelograms taken for unrelated causes. To summarize, while malignant renal tumor may be suspected in these cases, if the Papanicolaou test is negative, only by biopsy, short of pathologic examination after nephrectomy, can a certain diagnosis be made.

OPERATIVE TECHNIQUE

Preoperative study. In addition to a general examination cystoscopy and retrograde examination of the upper urinary tract with Papanicolaou stains of the divided urine are imperative. Whereas excretory urograms may arouse suspicion, in the diagnosis of early filling defects retrograde pyelograms provide more clear delineation. Since incision of the kidney is not justified without accurate localization of the suspicious area, lateral oblique, or stereoscopic views are required in addition to the anteroposterior pyelogram.

Exposure of the kidney. Because of the possible danger of disseminating tumor cells by manipulation the kidney should be exposed as gently as possible. Although some urologists believe that the pedicle can be secured with less trauma by the transperitoneal approach, in our experience there has been little or no additional operative manipulation by use of the lumbar route, particularly if the kidney is situated high and has a short pedicle. By resection of a rib, if indicated, and making a sufficiently long lumbar incision the organ can be delivered with minimal trauma. However, for those who prefer the transperitoneal route, there is no reason why this can not be used in renal biopsy.

In utilizing a lumbar incision manipulation is avoided by shunning the kidney during exposure. It is delivered chiefly by traction exerted on Gerot's fascia (fig. 1, A). Gerot's fascia is freed from its attachment posterior to the renal pelvis and stripped from around the kidney by the application of curved clamps. Working from the side of Gerot's capsule the perinephric tissues are separated from the kidney and as the kidney is delivered into the wound its isolation is facilitated by using gauze sponges as a hammock around the upper and lower poles (fig. 1, B). The upper extent of the ureter and the vascular pedicle are freed of all surrounding tissues. The pedicle is isolated for as long a distance as possible to facilitate the application of clamps if nephrectomy is found indicated.

Compressing the pedicle and ureter. If external examination of the kidney does

not disclose the cause of deformity in the pyelogram, the vascular pedicle and ureter are compressed and preparation made for incision into the kidney. A rubber-tipped clamp is applied to the upper portion of the ureter and a rubber tube is placed as a tourniquet around the vascular pedicle. An 18F Robinson catheter serves this purpose admirably. Since the pedicle in humans is large, a tourniquet provides added security by compressing any lymphatic chains which might lie in the hiatus at either extremity of a rubber-tipped clamp (fig. 5). The tourniquet is applied as close to the kidney as possible to permit the application of clamps distal to the point of occlusion if nephrectomy is found necessary. An assistant applies constant traction to the tourniquet and the wound is carefully protected with laparotomy tapes (fig. 6, 1).

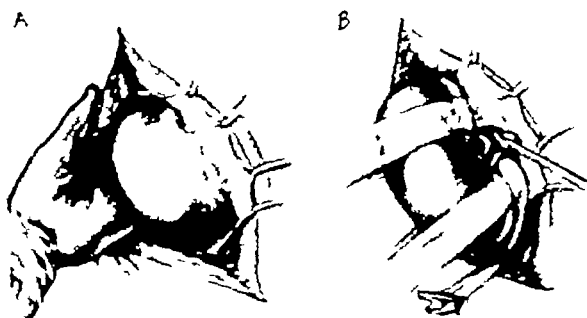


FIG. 4. A: Kidney being exposed with minimal manipulation by traction on Gerota's fascia. B: gauze used as hammock to aid in delivering kidney and isolating pedicle.

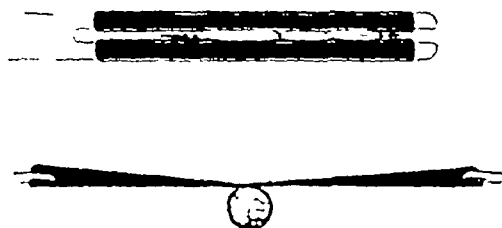


FIG. 5. A tourniquet is more effective than a rubber-tipped clamp in occluding perivascular lymphatics of renal pedicle.

Biopsy of the Kidney. After making a final inspection of the pyelograms which are displayed during operation, the suspicious area in the kidney is incised, usually along Broedel's vascular line, rather than in a transverse plane. In placing this incision, usually no help is derived from studying the external contour of the kidney or from palpation of the parenchyma. The incision may be made either with a scalpel or with a high frequency cutting blade (fig. 6, B).

When a cyst is present, the diagnosis is often evident as soon as the lesion is exposed and the interior inspected. However, if there is any suspicious area in the wall, a portion should be excised for microscopic study. When an apparent tumor is observed, deformations on the vast majority will prove to be malignant, but in a small number will be made unless a frozen microscopic section is examined. Of great examination, benign adenomas, and some infectious processes may

resemble malignant tumor. During biopsy great care is taken to prevent possible continuation of the wound and *compression is maintained* on the ureter and pedicle while frozen section is made.

Nephrectomy. Whenever the diagnosis of malignant tumor is established, the incision in the kidney is cauterized, closed with a running suture (fig 6 C) and the instruments used in making the biopsy are discarded. *Without releasing tension on the pedicle or ureter* clamps are placed distal to the point of occlusion in preparation for nephrectomy. One clamp is placed distal to the rubber-tipped clamp on the ureter, division of this structure being made between the two. Without releasing tension on the tourniquet, two pedicle clamps are placed as

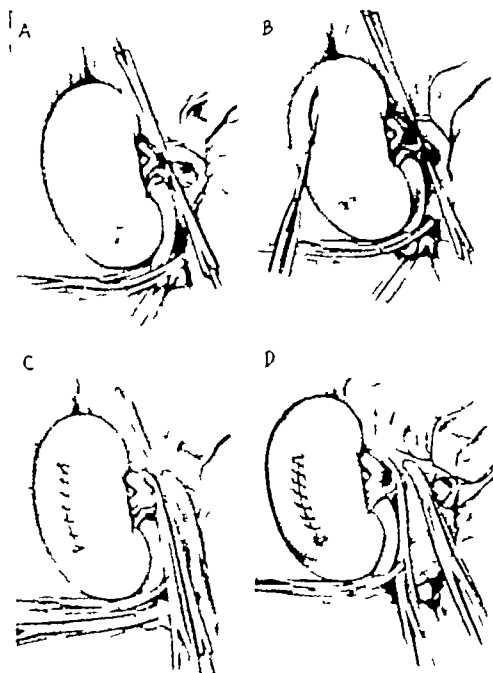


FIG. 6. A. Complete temporary isolation of kidney. Pedicle occluded with tourniquet, ureter with rubber-tipped clamp. Wound protected with lipirotomy tapes. B. Incision into precisely localized area. C. Preparation for nephrectomy in malignant tumor. Biopsy incision closed. D. Application of pedicle clamps without release of tourniquet. E. Amputation of kidney without escape of blood, urine or fragments of tissue. Ligation of pedicle and ureter.

far down on the vascular pedicle as possible, and a Peon clamp is placed close to the kidney. If there is insufficient room on the pedicle, this clamp may be applied directly over the encircling portion of the tourniquet. The pedicle is then divided by an incision made between the Peon and the two pedicle clamps. The ureter is ligated with a single suture of No. 1 chromic catgut, the pedicle with two ligatures of double No. 2 chromic catgut. This method assures removal of the kidney without escape of blood, urine, or fragments of tissue (fig 6 D).

After the kidney has been removed, all instruments and lipirotomy tapes used in this procedure are discarded, clean drapes applied, and the lumbar incision closed.

It is assumed that before performing nephrectomy preoperative studies have demonstrated the presence of a normal kidney on the opposite side. If the opposite member is absent or functionally insufficient, excision of the tumor with a rim of normal adjacent renal tissue should be attempted. Vermooten was able to accomplish this in one case of clear-cell carcinoma with apparent success.

Nephrotomy in benign lesions. In exploring the kidney the practice of aspiration is to be condemned. Recovery of fluid is useless as a diagnostic aid; furthermore, it is difficult to recognize a cystic area by incision after fluid has been evacuated.

If a cyst is discovered it should be opened widely and the interior carefully

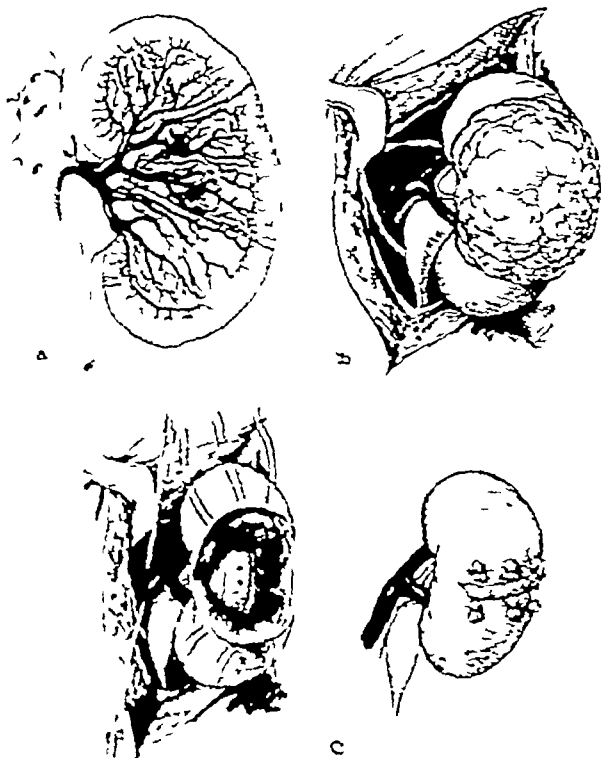


FIG. 7. *A*, diagram showing how midportion of kidney may be resected without danger to blood supply. *B*, multilocular cyst of midportion of kidney. *C*, method of excision.

examined to be certain that there are no irregularities of the lining indicative of malignancy.

The lining of a serous cyst usually separates easily from the contiguous parenchyma and the defect is closed as following heminephrectomy. In view of the radiating arrangement of the arcuate vessels out from the renal hilum, it is practically always possible to resect a benign lesion, even though it lies in the midportion of the kidney (figs. 7 and 8).

If no lesion is obvious when the kidney is incised, care must be taken to assure careful exploration. In any doubtful case it is advisable to incise down to and into a distorted calyx and to biopsy tissue from the suspicious zone indicated by pyelography.

In dealing with benign lesions of the parenchyma, a wedge-shaped incision facili-

tates closure and prevents development of urinary fistula. The incision is closed over a free fat transplant securing the area with mattress sutures of No. 0 chromic cutgut on anatraumatic needle (fig. 9, A). The suture material is prevented from cutting into the kidney by bolsters of fat (fig. 9, B).

ILLUSTRATIVE CASES

The following cases are presented to elucidate the foregoing discussion.

Case in which biopsy is not indicated. The first patient presents the problem of continued bleeding from one kidney without pyelographic deformity or other clue as to the cause of bleeding. This is an example of the type of case that is not suitable for biopsy.



FIG. 8. Operative specimen from clinical case in which opposite kidney was functionless.

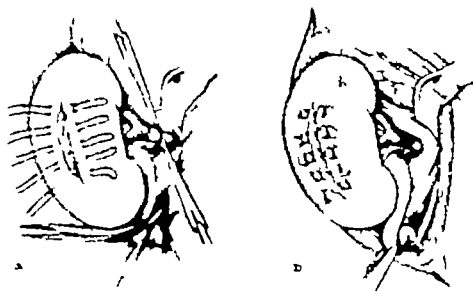


FIG. 9. Closure of nephrotomy in resection of benign lesions of renal parenchyma.

Case 1. A Negro, 30 years of age, when first examined complained of painless hematuria for 6 weeks. Physical examination revealed no abnormalities. Reported examination of the urine showed the presence of gross blood, a proportionate number of white blood cells and no bacteria of any type. Upon cystoscopy the bladder and urethra appeared normal but blood was invariably seen coming from the left ureteral orifice; urine from the right was always clear. Repeated retrograde pyelo-ureterograms, with oblique views, showed no abnormality of the kidney or ureter on either side (fig. 10). No systemic cause for bleeding was discovered. After observation for 2 months, during which time there were repeated periods of profuse hemorrhage not arrested by blood transfusions, vitamin therapy, renal lavage and other conservative measures, left nephrectomy was performed. Careful examination of the kidney, including microscopic study of serial sections, did not reveal any lesion to account for the bleeding.

This case is not unusual and typifies a small group of cases of obscure etiology in which the cause of severe renal bleeding is never determined. In similar cases microscopic lesions, such as papillitis or small hemangioma, are sometimes discovered after exhaustive search. The futility of renal biopsy in these cases is obvious.



FIG. 10. Case 1. Obscure bleeding from left kidney. Retrograde pyelo ureterogram shows no gross abnormality.



FIG. 11. Case 2. Right pyelogram shows a circular filling defect causing separation between the middle and caudal calyces.

Kidney needlessly sacrificed for benign lesion. In the next 2 cases the kidney was unnecessarily sacrificed for a benign lesion.

Case 2. A white man 61 years of age complained of right lumbar pain for 1 month. The only finding of clinical importance was a pyelographic deformity of the right kidney (fig. 11).

After a diagnosis of possible malignant tumor of the right kidney, transperi-

toneal nephrectomy was carried out. Externally the kidney appeared normal. On bisecting the organ a simple cyst was found in the location of the pyelographic deformity. There was no evidence of malignancy.

Case 3. A 64 year old white woman complained of a dull, aching left lumbar pain for 6 months. Results of all examinations were negative except for the

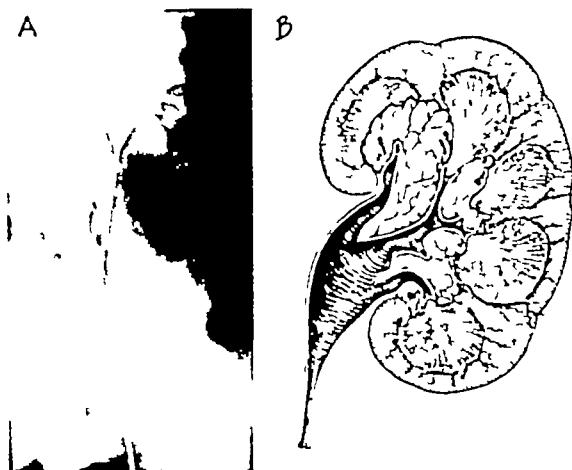


FIG. 12. Case 3. A, left pyelogram showing partial obliteration of cephalic calyces. B, following nephrectomy, deformity found to be caused by accumulation of peripelvic fat.



FIG. 13. Photomicrograph showing deformity caused by accumulation of peripelvic fat.

pyelographic findings (fig. 12, A). Another retrograde pyelogram 1 week later, showed identical changes. A diagnosis of malignant tumor of the left kidney was made, and lumbar nephrectomy was performed.

Externally the kidney appeared normal. On section the partial obliteration of the cephalic calyces was found to be caused by an abundance of peripelvic fat (figs. 12, B, and 13). The kidney was normal in all other respects.

Both of these cases were suitable for renal biopsy and in each instance the diagnosis could have been made at operation and the kidney preserved. The literature abounds with similar case reports.

Biopsy and preservation of kidney with benign lesion. In the following 5 cases (Nos. 4, 5, 6, 7, and 8) biopsy was carried out by the technique described, the opposite kidney in each instance was normal.



FIG. 11. (A) Retrograde pyelogram shows distortion of caudal minor calyx of right kidney. (B) Gross section of wall of cyst. No evidence of malignancy. (C) Position of cyst in the excision.

CASE 4. A 10-year-old white male complained of frequency and urgency of urination for 3 months. During diagnostic studies, which revealed non-specific cystitis, proctitis and urethritis as the cause of his complaints, an abnormality was observed in the right pyelogram (fig. 11, A). No neoplastic cells were found in the excised calyces of the lungs and skeletal system revealed no evidence of metastasis.

A diagnosis of possible renal tumor was made and the right kidney explored. Externally the kidney appeared normal. Upon incising the parenchyma in the

region of the filling defect, a cyst filled with clear fluid was entered. Careful inspection revealed the lining to be smooth throughout. A frozen microscopic section showed a layer of fibrous tissue without evidence of malignancy (fig. 14, B). The wall of the cyst was stripped out and an elliptical area of cortex incised around the nephrotomy in order to facilitate obliteration of the dead space (fig. 14, C).

CASE 5. A white man of 22 years had been hospitalized for several weeks to determine the cause of a persistently elevated temperature, which ranged from 99.6 to 100.6°F. The leukocyte count averaged about 10,000 per cu. mm. with 70 per cent polymorphonuclears. Upon the most exhaustive diagnostic studies, the only suspicious finding was confined to the left pyelogram. Excretory urograms first suggested a possible filling defect. On checking this finding by retrograde pyelography with lateral views, a separation was noted between the upper and lower calyces (fig. 15). This suggested a bifid renal pelvis, but in order to be certain that it was not caused by a renal tumor producing an elevation of temperature, as sometimes occurs, exploration was performed.



FIG. 15. Case 5. Left pyelogram shows separation of upper and lower calyces suspicious of a space-consuming lesion. A, anteroposterior and B, semi-oblique view.

The parenchyma in the region of the suspicious area was deeply incised. The incision was carried down to the renal hilum but not into the calyceal system. Tissue was removed and frozen section made, which showed normal parenchyma. This procedure assured the diagnosis of bifid renal pelvis, for if a tumor had been present which was sufficiently large to cause separation of the calyces it would have been discovered by this procedure.

When the patient was examined 1 year after operation, he was still running a fever. The final medical opinion was that his temperature elevation represented a normal variation. Excretory urograms after the year's interval showed no change.

CASE 6. A 42-year-old white woman was admitted to the hospital because of left upper abdominal pain associated with nausea and vomiting. Gastrointestinal studies revealed no cause for her complaints. The urine was normal. Excretory urography suggested a filling defect in the upper pole of the left kidney. Retrograde pyelograms with lateral views were more suggestive (fig. 16).

Upon exploration of the kidney no abnormality was found on the exterior surface nor was any lesion discovered upon incision of the parenchyma in the area of the apparent defect. The incision was deepened down to the peripelvic tissues which did not contain sufficient fat to produce the deformity and finally carried into the middle and upper calvices. Since any mass sufficiently large to produce such a defect would have been encountered, the irregularity was attributed to congenital variation.

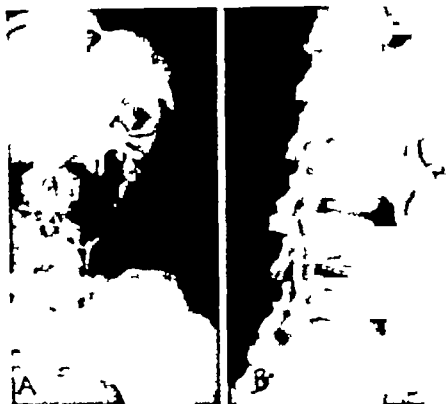


FIG. 16. Case 6. *A*, pyelogram shows elongation of cephalic calyx and downward displacement of middle calyx suggesting a space consuming lesion in upper pole left kidney. *B*, oblique view. (Note similarity to figure 19.)

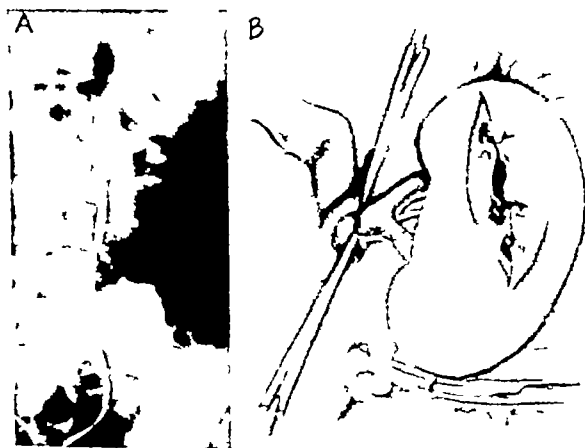


FIG. 17. Case 7. *A*, pyelogram shows separation of minor cephalic calvices of left kidney due to a space consuming lesion. *B*, nephrotomy through area of pyelographic defect. The cephalic calvices showed no abnormality.

CASE 7. A 48-year-old white male entered the hospital because of two attacks of painless hematuria during the week prior to entry. Urologic investigation revealed evidence of early benign prostatic hypertrophy and of a possible mass in the upper pole of the left kidney (fig. 17, *A*). A tentative diagnosis of carcinoma of the left kidney was made.

Upon exploration of the left kidney no suspicious area was noted on its external surface. The upper pole was incised in the region of the apparent filling defect

into the cephalic calyces (fig. 17 B). There was no evidence of any space consuming lesion or other abnormality, and the nephrotomy was closed. The final diagnosis was a congenitally malformed pelvis. Hematuria was attributed to benign prostatic hypertrophy.

Case 8. A 49-year-old white man complained of left lumbar pain for 2 days. The urine was normal. Cystoscopy revealed a normal bladder and urethra. Pyelograms showed distortion of the caudal calyx of the left kidney (fig. 18 A).

Upon exploring the left kidney the external surface appeared normal. Deep incision into the area of the apparent filling defect revealed no evidence of tumor, cyst or other space consuming lesion. Tissue excised for frozen section was reported as showing no abnormality other than arteriosclerotic changes. The final diagnosis was nephrosclerosis and anomalous formation of the pelvis.

This patient has been examined periodically for two years without change in pyelographic findings (fig. 18 B).



FIG. 18. *CASE 8.* A, preoperative pyelogram showing distortion of caudal calyx, left kidney. B, postoperative pyelogram taken 2 years later.

Diagnostic incision and nephrectomy for carcinoma of kidney. *Case 9.* A white man 35 years of age was found to have microscopic hematuria on routine physical examination. Upon urologic study the only abnormal findings were confined to the upper urinary tract. Cystoscopy showed smoky urine coming from the left ureteral orifice, and upon pyelography an apparent separation between the upper and middle calyces of the left kidney was noted (fig. 19 A and B). Roentgenograms of the lungs and skeletal system revealed no evidence of metastasis.

The clinical impression was carcinoma or cyst of the left kidney. When exposed in the usual manner the kidney appeared normal. Upon incising the parenchyma in the area of the pyelographic defect a yellowish lobulated mass was encountered 2 cm beneath the capsule (fig. 19 C). Its gross appearance was so typical of clear cell carcinoma of the kidney that frozen section was not made, and nephrectomy was performed according to the described technique.

Pathologic examination revealed a clear cell carcinoma of the cortex of the kidney, approximately 3 cm in diameter, surrounded by normal parenchyma.

fig 19 *D*: Sections showed no evidence of invasion of the renal pelvis, the capsule or the veins of the kidney

The patient was alive and well 5 years after operation without evidence of local recurrence or metastasis

This was one of our first cases of exploratory operation and in retrospect we believe that a frozen microscopic section should have been made to confirm the diagnosis made on the basis of the gross appearance of the lesion



Fig. 1. *A*, *B*: Pyelograms show separation of upper and middle calyces, left kidney, right kidney. *C*: nephrotomy showing tumor 2 cm beneath capsule. *D*: photomicrograph of clear cell carcinoma of kidney.

SUMMARY

Although biopsy of the kidney has been widely condemned as a hazardous procedure, we have attempted to develop a technique of biopsy which allows one to biopsy the kidney without danger and with the same confidence that one can biopsy other organs of the body. By the experimental use of radioactive tracer we have shown that with certain precautions there is little possibility of dissemination of tumor cells during this procedure.

In cases of a small pyelographic filling defect suggestive of tumor of the parenchyma in which the distinction between a benign and a malignant lesion cannot be made, the following procedure is carried out: 1) exposure of the kidney with as little manipulation as possible, 2) isolation of kidney by securing the vascular pedicle and upper portion of the ureter, protecting the wound with laparotomy tapes, 3) incision into the suspicious area demonstrated by pyelographic studies, inspection of the incised area with excision of tissue for frozen section, if indicated. On the basis of observations made during these procedures, decision is reached whether to perform 1) simple closure of the nephrotomy incision, 2) partial resection of the kidney for a benign lesion, or 3) nephrectomy in the presence of a malignant tumor.

The intelligent clinical application of the method will result in preservation of many kidneys which are needlessly sacrificed for benign lesions. The method has been performed in six cases in which the kidney appeared normal when exposed at operation. In five the lesion was benign, and in all five the kidney was preserved. In the sixth the carcinoma was found and nephrectomy carried out. The patient was well after 5 years.

The public and medical profession are constantly importuned as to the necessity for early diagnosis if cancer is to be cured. Unfortunately, in a large proportion of cases of cancer of the kidney there are no early symptoms. Yet one way to reduce an alarmingly high mortality is to urge early biopsy in cases of suspected malignancy. Procrastination in the presence of possible malignancy is to be condemned.

We believe that biopsy of the kidney should be recognized as a justifiable surgical procedure. The time has come to denounce the archaic teaching that if there is sufficient evidence to warrant operation for suspected malignancy, removal of the kidney is mandatory. Our opinion is that if the lesion is malignant, carefully executed biopsy can do no harm, if the lesion is benign, nephrectomy is too radical.

Cases 3, 6 and 7 are presented through the courtesy of Dr. Edmund P. Gaylor, Dr. Frederick Howard, and Dr. John W. Schulte.

Appreciation is extended to the Harold Brunn Cardiovascular Institute where some of the experimental studies were done.

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BILATERAL RENAL AGENESIA

HARRIS HAVIN

Although congenital anomalies of the urinary tract are by no means uncommon, bilateral renal agenesis is a rare abnormality exciting much speculation, discussion and controversy as to its etiology and clinical features.

In 1883 Coen¹ made the first serious attempt to assemble cases of bilateral renal agenesis and described 32 cases recorded in the literature to that date. In 1931 Rosenbaum² again reviewed the literature and after adding 1 case of his own brought the total to 91. Madisson³ in 1934 further accumulated case reports including 1 of his own to bring the total to 105 cases, but, unfortunately, he did not give specific reference to the one-hundred and fifth case.

In a critical review of the literature Amolsch⁴ in 1937 retabulated the number of case reports. He logically deducted case number 29 from Rosenbaum's series (cited from Coen's tabulation) because the patient lived 14 years. In addition, he deleted case number 105 from Madisson's group since there was no specific reference to it in Madisson's paper. He then added 4 cases of his own to those reported up to that time and enlarged the number to 119.

Hinman⁵ in 1940 reported 1 case, reviewed the literature, and amassed a total of 135 cases. However, Hinman made two incorrect calculations. First, in his summation, he quoted Amolsch's total as 116 instead of 119. Secondly, he incorrectly added 1 case reported by Bates⁶ claiming it was not included in Amolsch's series. To prove his point Hinman referred to the same publication by Bates that had been correctly quoted by Amolsch. In this controversial article by Bates 2 cases of bilateral renal agenesis were reported by the author, and another case described by Huerzeler* is cited. All 3 of these cases were counted in Amolsch's series. Making the necessary changes in Hinman's tabulation (deducting one and adding three) his total should have been 137 instead of 135.

The foregoing tabulations do not include the following: 1 case reported by Gunewardene⁷ in 1935, 1 case reported by Przeworski⁸ in 1936, and 1 case by Seidel⁹ in 1939. This brings the total to 140. In addition the following cases have been described since Hinman's article: 1 by Grimm¹⁰ in 1940, 3 cases by Nation¹¹ in 1941, 1 by Stokes¹² in 1944, and 20 by Potter¹³ in 1946.

No specific reference to Huerzeler's article was given by Bates, nor could one be found in the literature.

¹ Coen, J. *Annali Universitari di Med. et Chir.* **267**: 52, 1884.

² Rosenbaum, P. *Frankfurt. Ztschr. f. Path.* **41**: 136, 1931.

³ Madisson, H. *Centraltidn. f. Allg. Path. u. path. Anat.* **60**: 1, 1934.

⁴ Amolsch, A. L. *J. Urol.* **38**: 360, 1937.

⁵ Hinman, F. *Surg., Gynec. & Obst.* **71**: 101, 1940.

⁶ Bates, G. S. *Am. J. Obst. & Gynec.* **25**: 41, 1933.

⁷ Gunewardene, H. C. P. *Colon. J. Sci.* **3**: 23, 1935.

⁸ Przeworski, B. *Ginekologia polska* **15**: 775, 1936.

⁹ Seidel, E. *Kinderztl. Praxis* **10**: 489, 1939.

¹⁰ Grimm, K. B. *J. Urol.* **44**: 57, 1940.

¹¹ Nation, L. F. *Surg., Gynec. & Obst.* **79**: 175, 1944.

¹² Stokes, G. D. *Arch. Path.* **35**: 250, 1944.

¹³ Potter, L. L. *J. Pediat.* **29**: 68, 1946.

The pronephros undergoes progressive and complete regression but the mesonephros persists as rudimentary structures in the female or as the functional duct in the male genital system. The metanephros begins by budding from the terminal part of the mesonephric (wolffian) duct during the fourth week of fetal growth and then develops into a more complex system of ducts and tubules.

Brown¹² and Boyden¹³ have shown that the renalanlage can form without the development of the ureter. Brown demonstrated in mice that nephrogenic mesenchyme develops and forms in embryonic kidney in the complete absence of a ureter which was prevented from developing by the experimental arrest of the wolffian duct. Boyden obtained the same results in chicks. Although no determination was made of the eventual fate of the renal tissue in these animals it was fading in the oldest. Boyden also described a human embryo ten millimeters in length with a renalanlage on the side of an absent ureter (due to arrested development of the wolffian duct), but no tubular differentiation was evident. Rimer¹⁴ suggested that this differentiation is dependent upon contact of the ureter with the nephrogenic cup, and proper fusion is necessary for the complete development of the tubular system.

To further support Rimer's hypothesis that the differentiation of the nephrogenic cup depends on the stimulus produced by the growth of the ureteral bud into it is the fact that no cases are recorded of a completely formed metanephros in the absence of a ureteral bud. On the other hand, cases have been reported in which the ureteral structures or its remnants developed when no metanephros was formed. Furthermore the experimental work on chick embryos performed by Boyden¹³ and Gruenwald¹⁵ and the anatomic findings in human embryos described by Kornfeld¹⁶, Auër¹⁷ and Gruenwald¹⁴ also support this theory.

Thus renal agenesis can be caused by either of two factors: 1) a hereditary or mutational defect in the germ plasma affecting the ureterogenic area, the metanephrogenic tissue or bothanlage or 2) developmental arrest caused by some mechanical or other type of blighting factor effective at various stages of development and in various uteri. Madisson's report³ of bilateral renal agenesis occurring in two siblings (not twins) supports the former theory, while his and the author's report of this finding in only one of twins does not definitely negate it if the twins are dizygotic. However, if the twins cited in this article are accepted as being truly monozygotic the second theory is confirmed. In addition the experimental work of Stockard¹ is further substantiating evidence in favor of the latter theory.

CASE REPORT

Mrs. A. M. service of Dr. Hans A. Abraham, a pregnant multiparous 23 year old white woman was admitted at term to Jewish Hospital Philadelphia. Her previous two pregnancies had been uneventful, and both children were normal full term infants with no congenital anomalies. During this present

¹² Brown, A. A. *Am. J. Anat.* **47**: 117, 1931.

Boyden, E. A. *Anat. Rec.* **52**: 32, 1932.

Kent, A. B. *Strgo. Path. Anat. u. 7. dle Path.* **87**: 137, 1931.

Gruenwald, P. *Arch. f. Entw.* **136**: 786, 1937.

¹⁶ Kornfeld, W. *Anat. An.* **60**: 497, 1926.

pregnancy -he was examined regularly prenatally and her prenatal course was without complications. On July 22, 1949 the patient went into labor and with the aid of light general anesthesia spontaneously delivered a pair of unimolar male twins sixteen minutes apart. The umbilical cords of the infants were attached to a single placenta.

The first infant weighed 8 pounds 3½ ounces, was 21 inches in length and breathed easily and normally immediately after birth. There were no abnormalities apparent.

The second twin weighed 5 pounds 10 ounces, was 18 inches long and had no apparent congenital anomalies at birth. However respirations were labored, shallow and irregular from birth and pallor alternated with cyanosis. The infant's cry was weak. The lungs expanded only slightly with inspiration and breath sounds were hardly audible. No rales were present. The heart sounds were of good quality and no murmurs were heard. The cardiac rhythm was normal. Extreme moulding of the head was observed. A Moro reflex could not be elicited and the grasp reflex was weak bilaterally. All the other organs and systems appeared normal. A tentative diagnosis of neonatal asphyxia due to intracranial injury was made at that time.

The upper respiratory tract of the second twin was aspirated gently but thoroughly. The infant was placed in a heated crib in a horizontal position and oxygen by funnel at the rate of 6 liters per minute was administered. Even with this therapeutic regime the respirations became more irregular and labored and the color poorer. Caffeine and sodium benzoate (1½ gr.) were administered twice hypodermically without beneficial effect. Despite these measures plus artificial respiration the clinical condition steadily deteriorated. The cyanosis increased and the respirations became more labored, shallow and irregular. The infant ceased breathing three hours and one minute after birth.

At autopsy the corpse was described as a full term cyanotic newborn with no external anomalies. The lungs showed bilateral atelectasis. Patency of the ductus arteriosus and on the foramen ovale of the heart were noted. Both kidneys, bladder, etc., and the bladder were absent. The penis was normal in size but no urethral opening was present. The central nervous system, digestive system and uro-genital system were all normal.

On histological examination the lungs were found to be immature and the degree of bilateral atelectasis was confirmed. The spleen was congested. The testes showed slight immaturity but the epididymides were normal. No abnormalities were found. Each adrenal had a well-developed cortex, a moderately cellular medulla and extremely scanty medullary tissue. The thymus was normal.

A tentative diagnosis of bilateral atelectasis, congenital absence of the kidneys, and of the bladder, and of slight immaturity of the testes.

The still-born twin of the twins so died within the first 24 hours of life.

He was autopsied as reported in all reports and in November 1950 the report was that the infant had died with no evidence of any congenital

ASSOCIATED CLINICAL AND PATHOLOGICAL FINDINGS

Potter¹ collected extensive clinical data concerning her 20 reported cases of bilateral renal agenesis. No causative relationship was found to the method of delivery, parity, maternal age, or complications of pregnancy. Of those infants born alive, cyanosis or other respiratory difficulty was present in all cases, and in some respirations could not be established. In her series the causes of death were the following: asphyxia in 11 cases, congenital malformations in 8 cases, and intracranial hemorrhage in 1 case.

Potter also observed two anomalies in almost all these cases that were not noted previously: hypoplasia of the lungs and abnormal but characteristic facial expression. This peculiar prematurely senile facies was described as showing an increased space between the eyes, a prominent fold which arose at the inner canthus and swept downward and laterally below the eyes, an unusual flattening of the nose, excessive recession of the chin, and moderate enlargement and decreased chondrification of the ears. These facial features have not been corroborated by the case reported here.

Although bilateral renal agenesis is incompatible with life, the causes and time of death differ from what might be logically anticipated. Absence of the kidneys would lead one to expect death from signs and symptoms of renal failure in most cases. However, in none of the 166 reported cases was the cause of death attributed to renal failure. In addition, all these infants except 2 were stillborn or died within 12 hours after birth. Of the 2 exceptional cases, one lived 11 days and the other 21 days, both dying of extrarenal causes. These facts lend credence to the theory that nature tends to stifle life early in those physically incapable of adjusting to extrauterine existence.

The incidence of bilateral renal agenesis in the various sexes has changed relatively little over the years. When Amolsch¹ reported in 1937 on the first 119 cases recorded in the literature, he discovered that most cases occurred in males (63 in males, 24 in females, and 32 unclassified as to sex). Since that time the majority of cases reported have also been in males, and now the disparity in the sex incidence has been slightly increased. Of the 168 cases now in the literature, 95 are in males, 31 in females, and 42 unclassified as to sex. This is a ratio of 3.07:1 of males to females, only slightly different from the ratio of 2.7:1 reported by Amolsch.

The observation has been frequently made that congenital anomalies tend to be multiple, and in this respect bilateral renal agenesis is no exception. In fact, renal agenesis is usually associated with gross malformations of other organs. In Humm's article² he states that in only 11 cases (8 per cent) out of 135 were abnormalities limited only to mesonephric and metanephric derivatives. In the case reported here anomalies of the genital system and bladder were associated with the absent kidneys and ureters.

Abnormalities of the lower extremities are especially common. Amolsch¹ listed 30 cases of sirenomelus, 2 of apus, 8 of monopus, and 32 with lesser deformities. The terminal large bowel is usually underdeveloped, and the anus is usually impotent.

Frequently there is an associated dysplasia of the genital system in both sexes. In the male the deficiency in the internal genitalia frequently involves mesonephric structures (wolffian duct system). In the female portions of the müllerian duct derivatives are usually present although definitely hypoplastic and frequently abnormal. The external genitalia are completely unformed or rudimentary in most cases but in some are well developed.

Associated anomalies of the remainder of the urinary system are frequently encountered. Although the bladder is often normal, in most cases it is either hypoplastic or definitely absent. The ureters are usually absent bilaterally but in 7 cases cited by Amolsch⁴ rudimentary ureters were present, and in 4 of these cases renal elements could be identified microscopically.

Other abnormalities may be found with bilateral renal agenesis but they are less common. Although the adrenal glands assume flat discoid shapes in the absence of the kidneys they are usually in their normal location and are rarely abnormal. Acromia, hydrocephalus, spina bifida, meningocele, microphthalmia, cardiac abnormalities, splenic deformities, anomalies of the upper gastrointestinal tract and other malformations of the musculo-skeletal system have occasionally been found associated with bilateral renal agenesis.

SUMMARY

The literature concerning bilateral renal agenesis is reviewed here. A case of this anomaly is described in the second born of uniovular male twins. Adding this case to the others previously reported in the literature brings the total to 168. The etiology of this condition is discussed at some length and the associated clinical and pathological findings are also presented.

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METASTATIC MELANO-EPITHELIOMA OF THE URINARY BLADDER: REPORT OF A CASE

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Metastatic neoplasms constitute a very small percentage of tumors of the urinary bladder. Metastatic involvement of the bladder by melano epithelioma apparently is rare; we have encountered only 3 such cases in a cursory review of the literature.

Way and Light reported a case of generalized melanosis in which necropsy revealed almost every organ of the body to be involved from a primary melano-epithelioma of the skin. The urinary bladder was described as showing extensive involvement.

McComb and Smith reported a case in which tumor of the bladder was treated by segmental resection. Microscopic examination disclosed melano epithelioma. A search was made for a primary lesion, but none could be found. The patient died 13 months after operation, and necropsy showed both adrenal glands to be involved with what was presumed to be the primary lesion. At this time, numerous subcutaneous metastatic lesions also were demonstrable.

Whelock reported 4 cases of sarcoma and 1 of malignant melanoma of the urinary bladder. The author included the case of melano epithelioma because at the time it was believed that melanomas were of connective-tissue origin. The tumor was treated by suprapubic implantation of radon seeds, followed by deep roentgen therapy. The patient died 7 months after operation. Postmortem examination was not carried out, and no primary lesion was demonstrated before death; therefore, the author speculated that this lesion may have been primary in the bladder, having its origin from an embryonic cell rest.

In the case we are presenting here the diagnosis was suspected preoperatively and was confirmed by biopsy. Because of the rarity of such a lesion, we feel that it is worth while to report this case.

REPORT OF CASE

A man 47 years old was first seen in the Mayo Clinic in October 1948. His chief complaint at this time was persistent drainage from the base of the nail of the right great toe. He stated that in July 1947, he had first noted a small amount of drainage from the base of the nail of this toe. There was no pain associated with the lesion. The patient consulted his physician, after a trial of local therapy, the nail was removed, and the nail bed was cauterized. This was followed by

complete healing in 2 weeks. No other symptoms were noted until a short time prior to his examination at the clinic. The family history and the patient's history were noncontributory.

Physical examination disclosed a healthy man 5 feet 11 inches in height weighing 171 pounds. The blood pressure, pulse, respiration and temperature were normal. The right great toe presented a granular-appearing lesion on the lateral aspect of the nail bed. The nail had been removed surgically. There was a slight amount of purulent drainage from the lesion, but the toe was not tender. There were several enlarged, nontender nodes in the right inguinal region. The edge of the liver was palpable, but was not tender. Results of physical examination otherwise were negative.

Laboratory studies revealed the urine and blood to be normal. The erythrocyte sedimentation rate was 30 mm. in one hour by the Westergren method.

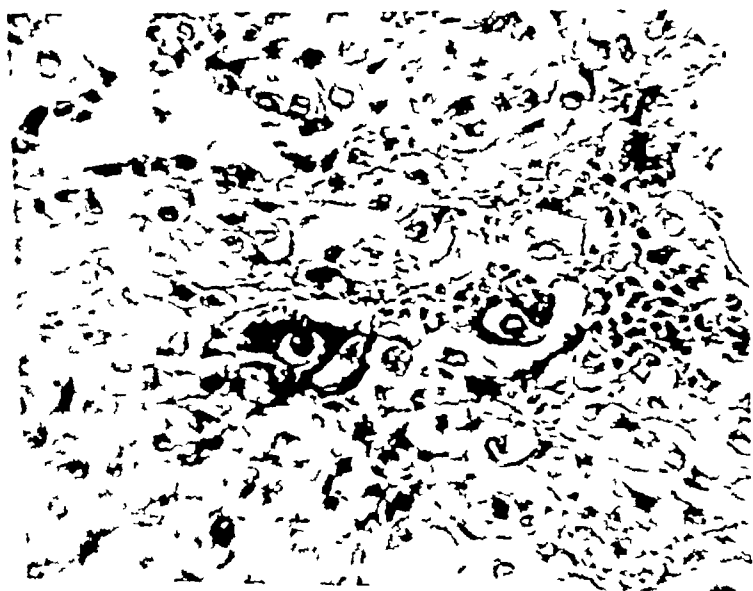


FIG. 1. Metastatic melanoma-epithelioma of urinary bladder. Histologic section of lesion stained with hematoxylin and eosin. (H&E) (reduced from original magnification of 100 times).

Results of tests of hepatic function all were within normal limits. As was the case with the flocculation test for syphilis. Roentgenologic examination of the chest failed to show any pathologic lesion of the bones. A roentgenogram of the pelvis showed no significant abnormality.

A skin biopsy was suspected. For this reason, the right inguinal lymph node was removed and the right great toe was amputated. Pathologic examination of the amputated subungual melano-epithelioma involving the nail bed and the right inguinal lymph node also showed metastatic melanoma.

At the time of his last examination, December 1949, the patient returned to the

clinic Examination disclosed a metastatic lesion which involved the skin on the medial aspect of the right thigh. The lesion was excised and deep roentgen therapy was administered to the right thigh.

On January 22, 1950, the patient was seen in urologic consultation because of terminal hematuria which consisted of only one drop of blood on one occasion. He had no other symptoms referable to the urinary tract. Results of routine urinalysis were negative except for microhematuria graded 1. Results of examination of the prostatic secretion were considered to be negative. On cystoscopic examination a small nodule 0.5 cm. in diameter was seen high on the posterior wall of the bladder. It was noted that this lesion did not have the typical appearance of the usual tumor of the bladder, and that it was somewhat blue containing several dark granules in its substance. Bimanual examination gave negative results. Bilateral pyelograms were considered to show nothing abnormal. Specimens were removed for microscopic examination, and the lesion was fulgurated. Microscopic examination of the excised specimen disclosed a malignant neoplasm in which melanin pigment was present in the tumor cells (fig. 1). The microscopic appearance was identical to that seen in sections obtained from the primary lesion of the great toe. A diagnosis was made of metastatic melanoepithelioma.

SUMMARY

A cursory review of the literature reveals only 3 cases in which the urinary bladder has been secondarily involved with melano-epithelioma. In 1 case there was a necropsy report of generalized melanosarcoma; in the other 2 there were primary vesical symptoms apparently caused by single melanomas of the bladder. The primary lesion in 1 case was located in the skin, in the second case it was felt to be primary in the adrenal glands; in the third no primary lesion was demonstrated. To the literature we have added an additional case in which the primary lesion was a melanoepithelioma of the great toe.

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behavior included masturbation, tantrums, and habitual and intentional encopresis (defecating in bed). In another girl equally problematic, bladder control was bought by rewards.

In older cooperative children control is usually acquired much earlier than in the young, its acquisition may further be stimulated postoperatively by practice of the start and stop urinary exercises wherein the patient, as he voids, stops the stream and starts, again stops and starts, until he has emptied his bladder. Thus the patient learns to exercise new sphincter control and becomes conscious of the desire to urinate and of the associated mechanics of bladder emptying. In these cases perfect control is rarely achieved until the cooperative patient becomes fully conscious of what is expected of him. While most of these patients show nearly normal control immediately or soon after operation, we do not consider them cured until they have perfect control, both day and night and the urine is sterile.

When a satisfactory sphincter cannot be reconstructed, and thus merits at least two trials, and if the rectal control is normal, ureterosigmoidostomy must be considered but to be employed only as a last resort. Thirteen of the author's fifteen cases were operated upon with satisfactory results with the exception of one operated upon at twenty-one months of age and who can hold his urine all night but leaks when up and about, reoperation will probably be necessary. One child, a boy of 14 months, died postoperative, today's improved supportive care would have saved him (fig. 3).

In one instance of penile epispadias treated by the Browne method the penile canal healed soundly but the urethral segment of the glans reopened, and will require subsequent closure. In another boy operated upon by Young's method (case 4), a dorsal urethral fistula required secondary closure (fig. 6).

SUMMARY

The salient features as observed in 15 personal cases of epispadias are discussed. When incontinence exists, adequate attempts should be made by plastic surgery to instate normal bladder control before ureterosigmoidostomy is seriously considered. In the 11 cases with complete urinary incontinence here reported, normal control and bladder function were achieved in 7 with good nocturnal but partial diurnal control in 1, one died postoperative, and in 2 operation was refused.

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The operation which I devised is a modification of Bucknall's operation. The Bucknall operation had much in its favor, but there was one fault, namely, that in using the skin of the scrotum to form a part of the urethra, hair grew into the urethra and calculi formed on these hairs. It, therefore, occurred to me that it was not necessary to use any skin from the scrotum whatsoever, and so I devised an operation in which the urethra was formed from the skin of the penis and this was then buried in a midline incision in the scrotum. In cases of bifid scrotum or perineal hypospadias, a layer of deep scrotal tissue is inter-

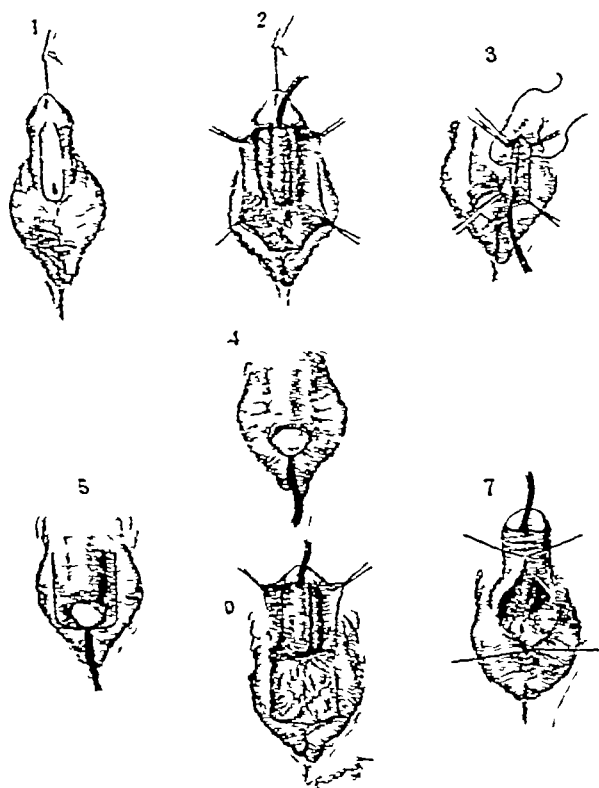


FIG 2 Ceeil operation for hypospadias

posed to cover the scrotal segment of the new channel (Culp). The steps of this operation are illustrated in figures 2, 3 and 4.

The sutures used for constructing the tube are 4-0 plain catgut, and this same material is used for fastening the penis to the subcutaneous scrotal tissues. The skin layer is closed with interrupted silk. At the conclusion of the operation sulfa powder is dusted on the wound and no dressing is applied.

Culp's report last year before the American Urological Association on the use of this operation is one of the most comprehensive reports that has ever been published on the cure of hypospadias. Among the cured cases reported by Culp were 5 patients who had had two or more failures in the construction of the

EVALUATION OF OPERATIONS FOR HYPOSPADIAS

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Hypospadias is a common developmental anomaly of the male external genitals. It is characterized by 1) ventral incurvation of the penis, produced by bands of fibrous tissue occupying the position of the undeveloped corpus spongiosum and 2) an ectopic urethral meatus, which may be located at any point on the undersurface of the penis from the prepuce to a position just back of its normal location in the glans penis. Treatment, therefore, consists in first correction of the penile deformity and later construction of the urethra. In 70 per cent of cases the ectopic meatus is on the ventral surface of the glans at or just behind the coronal sulcus and no treatment is indicated except in the occasional case of a stenotic orifice, which should be dilated or incised. In the remaining 30 per cent there is a varying degree of ventral deformity which must be corrected by removal of all constricting bands as a preliminary to construction of the urethra at a later date.

THE STRAIGHTENING OPERATION

The straightening operation should be done when the child is between 18 months and 2 years of age if he is seen during that time. The reason given for performing the straightening operation early is that it affords the corpora cavernosa a better opportunity to develop. On the other hand, we have obtained a perfectly straight penis with normal sexual function when the operation was done on patients up to the age of 32 years. This is not offered as a reason for delaying the operation but to point out that good results can be obtained at any age. It should be emphasized that correction of the chordee is equally as important as construction of the urethra. Unless this is successfully done, sexual function will be impaired or rendered impossible.

The operation is relatively simple but meticulous attention must be directed toward removal of all fibrous bands that may be contributing to the chordee. Some of these lie lateral to the midline, many are flat and almost transparent and consequently easy to overlook, and some are located in the intracavernous septum.

This operation may be done by either of two methods. The first utilizes the Hemeke-Mikulicz principle first used by Duplay in 1874 in which a transverse incision is made across the ventral surface of the penis just proximal to the glans and carried well into the prepuce on either side. Traction on the penis exaggerates the constricting bands so that they are easier to identify and remove. Buck's fusion and the intracavernous septum may be incised but injury to the corpora cavernosa is to be avoided. The wound is closed longitudinally.

The second method was first described by Edmunds and later by Blair; more recently it has been modified by Nesbit. It is especially applicable to the occa-

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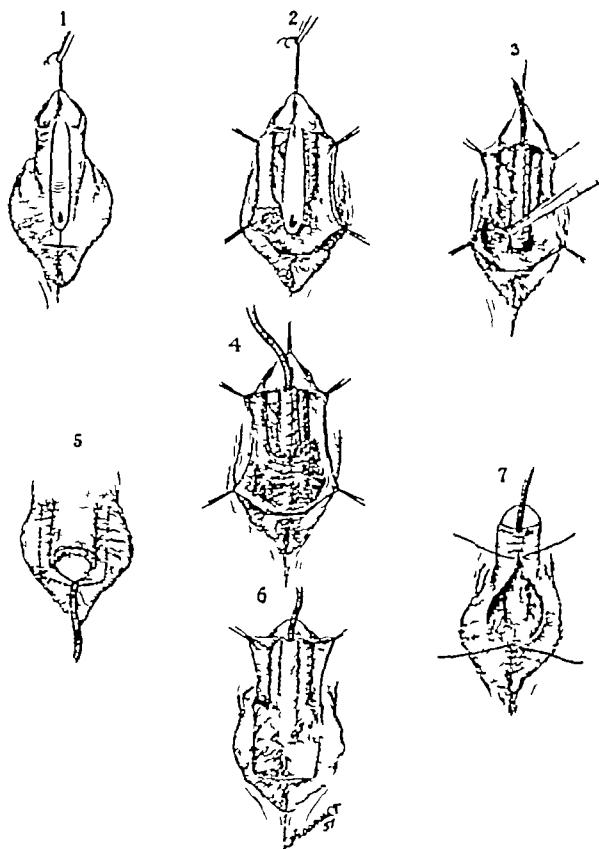


FIG 3 Cecil operation to be used in cases of bifid scrotum or perineal hypospadias

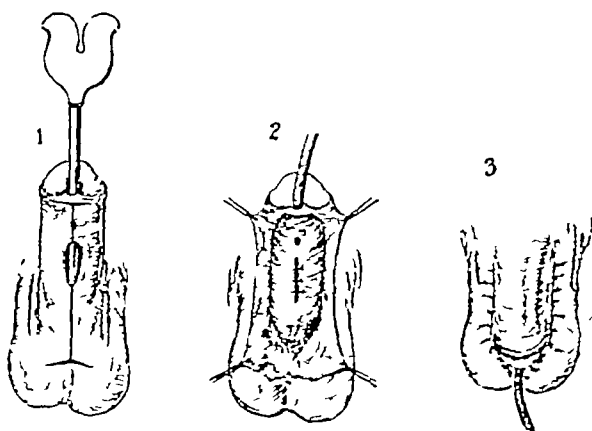


FIG 4 Cecil operation for urethral fistulas

urethra, and 1 patient who was cured after 9 previous operations. The operation is not only one of the most satisfactory for the cure of hypospadias but, as I have previously pointed out, for cure of urethral fistulas. It will undoubtedly play a large part in the treatment of war injuries of the urethra.

sional case in which the fibrosis may involve the skin on the ventral surface of the penis requiring its removal. In such cases the prepuce is freed, button-holed and swung over to cover the ventral defect. Attachment of the penis to the abdomen for a week or ten days, as advocated by some, is probably not necessary if all fibrous bands have been removed. Neither is diversion of the urinary stream indicated in connection with the straightening procedure.

CONSTRUCTION OF THE URETHRA

The question always arises as to how much time should elapse between the straightening operation and construction of the urethra. If the straightening operation is done in patients between the ages of 18 months and 2 years, it has been our recent custom to construct the urethra when the child is 4 or 5 years old. The small size of the penis in some children may necessitate a longer delay. In the older age group we believe that at least a year should elapse between the straightening procedure and final repair. It has been shown, and we have demonstrated in some of our own cases, that about a year is required for the scar tissue incident to the first operation to become soft and elastic and for the maximum blood supply of the tissue in this area to develop.

Diversion of the urinary stream. It is our belief that the urinary stream should be diverted regardless of the method used to construct the urethra. Perineal urethrostomy, in our opinion, is preferable to suprapubic cystostomy. However, in an occasional patient with perineal hypospadias there may not be enough room between the triangular ligament and the ectopic meatus to permit insertion of a perineal tube and in such cases suprapubic cystostomy would be the only method. The method described by Denis Browne and Cecil is certainly simple. After the perineal catheter has served its purpose and is removed, the fistula closes within 24 to 48 hours frequently with no leakage of urine whatsoever.

Techniques for construction of the urethra. A satisfactory method for construction of the urethra should fulfill the following requirements. First, it should be applicable to all degrees of the deformity, secondly, the urethra should be free from hairs and of approximately normal size and elasticity, thirdly, the operation should be capable of completion by the time the child first goes to school, fourthly, it should be simple enough for consistent performance by any reasonably capable surgeon and finally, it should conform to all the basic principles of plastic surgery.

A review of the literature reveals that no less than 148 surgeons claim originality in operations for repair of hypospadias. However, analysis of these operations indicates that they are all based upon five general principles. The first of these makes use of free grafts taken from extragenital sources, according to the method originally described by Nové-Josserand. Split thickness skin grafts are applied by a tunneling technique. The ureter, appendix, veins, vaginal mucosa and bladder mucosa have all been substituted for skin and to each of these procedures the name of the operator has been attached. The necessity for precision in preparing the graft, the difficulty of insertion and fixation, the problem of maintaining uniform pressure on the graft in apposition with the side walls of the tunnel and the accumulation of small blood clots provide the reasons for failure in enough cases to warrant discarding this method.

Denis Browne has recently revived an operation that was first described and illustrated by Duplay in 1880 and again in 1886, and was reviewed by me in 1936 in *Modern Urology* edited by Cabot. Duplay first originated the idea that a strip of skin left on the ventral surface of the penis, not made into a tube, would when enveloped by broad-bearing lateral flaps develop a urethral tube. He pointed out the value of broad-bearing surfaces in wide dissection of the lateral flaps. He used single sutures which were doubly locked, the single sutures not cutting holes as would loops, and sutured the skin edges with fine catgut. He described the dorsal relaxing incision. Duplay reported 5 cases that he had cured by this method. Burns has recently reported a series of cures in which he used the Denis Browne operation.

Any operation founded upon the four principles which I have stated will bring about the cure of hypospadias. It is my opinion that no operation will be so uniformly successful at all ages and in all cases, both in hypospadias and in the cure of urethral fistulas, as the technique which I have described.

Any operation that requires a child to be in the hospital more than 9 days, or that requires postoperative dilatation, or that results in fistulas, is not a modern operation for hypospadias.

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The second principle involves stretching the freed up urethra to the end of the penis according to the method of von Hacker-Beck. This operation is obviously confined to repair of minor degrees of hypospadias. Ritchie pointed out that in mobilization of the urethra into a single ended pedicle flap consideration must be given to maintenance of the blood supply. In addition to the possibility of slough, stretching the already short urethra may increase the ventral deformity and interfere with sexual function. We believe that this method should be discarded in favor of methods that better fulfill the requirements of the deformity.

The third principle is concerned with use of pedicle grafts from the penis or prepuce to build the urethra and use of penile skin to cover the defect.

a) In Cecil's adaptation of the Thiersch-Duplay principle for penoscrotal hypospadias the urinary stream is diverted by perineal ureterostomy and the operation is completed in one stage. In the case of perineal hypospadias, the urethra is constructed down to 1 cm. of the ectopic meatus. After healing is complete, the perineal opening is closed as a second step, according to the method of Duplay. The urinary stream is diverted by suprapubic cystostomy for the final repair. By this method the urethra is constructed entirely of hairless penile skin except in the perineal type. The flaps have a broad base and maintain an adequate blood supply. Staggering of the suture line decreases the frequency with which fistulas occur. The new meatus is at the level of the coronal sulcus. Excellent results are reported in the majority of patients operated upon by this method.

b) One of the first examples of a tube graft was described by Rochet. The tube was made from scrotal skin with its attached base proximal to the ectopic meatus. The tube was then drawn through a prepared tunnel to the tip of the glans penis. The new urethra has the obvious objection of being constructed of hair-bearing skin.

c) The method of D. M. Davis utilizes a tube graft made from the skin on the dorsum of the penis. The penis is bent dorsally so that the entire length of the tube can be utilized. A tunnel is made through the glans to the ventral surface of the penis and enlarged until the tube can easily be drawn through it and extended directly to the free end of the ectopic meatus. The dorsal end of the tube is freed in about two weeks if healing appears complete at that time. The meatus is situated at the apex of the glans. This method is not applicable to the more severe grades of hypospadias unless combined with some modification of the Thiersch procedure. Tunnels made through the glans penis have a tendency to contract and periodic dilations may be required.

A variation of this method is utilized in the Thompson-Russell operation in which the urethra is constructed from the prepuce and skin on the ventral surface of the penis. The base of the flap should be left broad in order to maintain an adequate blood supply. This method is not applicable to the more severe grades of the deformity. A considerable amount of penile skin on the ventral surface of the penis is utilized in forming the tube. The remaining amount of penile skin available to cover the defect without undue tension will further limit the usefulness of this method.

d) Ombredanne's method, known as the slit operation, consists in forming a

EXCRETORY UROGRAPHY IN THE DIAGNOSIS OF URETEROPELVIC OBSTRUCTION

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Urologists in general appear to favor retrograde pyelography over excretory urography in establishing a diagnosis of congenital ureteropelvic obstruction. This preference for retrograde study may be explained on the basis of the urologists' dissatisfaction with the delineation of the renal pelvis in the presence of hydronephrosis as obtained in the routine excretory urographic series. Certainly retrograde urograms yield, in most instances, clear-cut and decisive information about the interior of the normal as well as the diseased kidney. Despite this pictorial superiority of the retrograde urogram, inherent dangers exist in the execution of the procedure. The hazards of retrograde urography are well appreciated, and discussion about them between urologists is not infrequent. Nevertheless, the urologic literature records but few voices raised in protest against the indiscriminate use of retrograde urography in the study of the upper urinary tract. Such a one, however, was Prichard, who in 1945 stated: "Patients who have had both types of urograms (retrograde and excretory) prefer the intravenous, many have experienced pain, perhaps some shock, nausea and vomiting or hematuria, or perhaps a previously latent infection has been lighted following the retrograde procedure, demanding surgical drainage."

It would appear eminently desirable, therefore, to make the excretory urogram a more precise diagnostic tool in the presence of ureteropelvic obstruction. The purpose of this paper is to present a modification of the usual technique of obtaining excretory urograms which, in selected patients, will enable the genitourinary surgeon to make a diagnosis of ureteropelvic obstruction without resorting to retrograde injection of contrast medium into the renal pelvis.

MODIFIED TECHNIQUE

In order to present the basis for this excretory urographic technique, we will review a few of the physiologic and physical phenomena involved.

The contrast media commonly used in excretory urography are organic compounds containing iodine. It is the density of the iodine ions in the excreted urine which, by absorbing the roentgenographic rays, creates an image on the roentgenographic film.

Baumrucker and Prichard in separate articles have pointed out that following the intravenous injection of iodine-containing contrast media the specific gravity of the urine may rise as high as 1.065. Because of its high density, the urine containing the iodine compound will gravitate to the most dependent part

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of the new urethra by gathering up the skin proximal and lateral to the ectopic meatus by means of a purse string suture. The defect is then covered with the prepuce, which is button-holed and brought over the glans. Although the cosmetic effect of this operation is not ideal, the functional result is highly successful. The new channel is seamless and fistulous formation is obviated. The disadvantage is that it is applicable only to the distal penile hypospadias.

The operation involving the fourth principle was first described by Bidder in 1892 and was slightly modified by Bucknall in 1907. It utilizes a combination of scrotal and penile pedicle flaps to construct the urethra. Bidder's operation consists in forming the urethra with both penile and scrotal skin, the former forming the roof of the urethra and the latter the floor. Parallel incisions are made on the ventral surface of the penis and extended for an equal distance on the scrotum. The flaps are dissected up for a short distance laterally so that they may be sutured. After the wound has entirely healed, the penis is liberated from the scrotum, carrying with it the newly formed urethra. The scrotal defect is easily covered with adjacent scrotal skin. This method is applicable only to penoscrotal hypospadias, and has the disadvantage of hair-bearing skin that forms the floor of the canal. However, it may be utilized after other plastic repairs have failed and there is inadequate penile skin to construct the canal.

In Cecil's modification of the Bidder-Bucknall operation the urethra is constructed from a nonhair-bearing area. This is applicable only in cases in which an adequate amount of penile skin is available.

e) Finally, the Denis Browne operation is based upon the principle of use of a strip of intact skin which acts as a nucleus from which epithelium grows to line the newly formed urethra. After the straightening operation has been performed, this operation is a one stage procedure which involves several distinct steps.

1) Perineal Urethrostomy. A Malecot catheter is inserted into the bladder on a sound, the sound is partially withdrawn and its curve reversed so that it points in the perineum. With a diathermy knife a short incision is made over the point until the catheter is exposed. It is then grasped with a forceps and its distal end drawn through the opening. Gentle traction is placed upon the catheter until its wings are felt against the internal sphincter. It is tested with an irrigating syringe to be sure that its position is such that the bladder will be kept completely empty. As soon as this has been determined, the catheter is fixed in position by sutures.

2) Two parallel incisions made along the ventral surface of the penis are brought together immediately behind the ectopic meatus. This outlines the strip of intact skin which constitutes the nucleus from which epithelium lines the tube. The width of this strip will vary with each individual case and its diameter should be approximately the diameter of the average urethra for that age group. A triangular area of epithelium is removed on either side of the glans penis.

3) Whole thickness flaps are dissected laterally for a sufficient distance to allow their approximation without tension. Bleeding encountered during this stage of the operation is chiefly oozing. Only obvious bleeders need be ligated and these with the finest possible catgut. Two stab wounds are then made in the scrotum, posterior and lateral to the posterior angle of the wound and the tissues

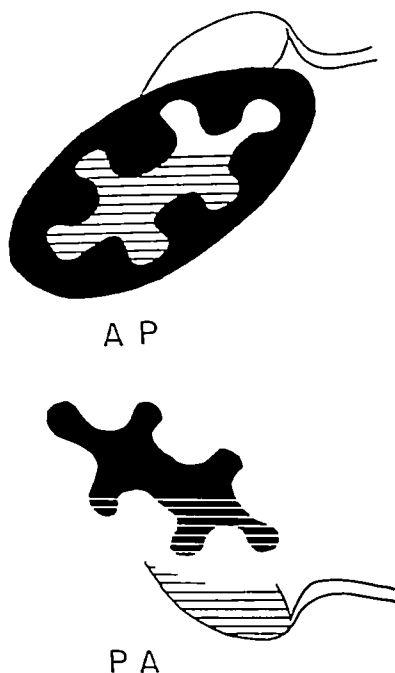


FIG 1 A, (upper) in patients with ureteropelvic obstructions who are lying supine, greater part of contrast medium-laden urine fills upper portion of kidney and renal pelvis may not be well outlined by roentgenography.

B, (lower) With patient prone urine containing contrast medium gravitates into pelvis, and area of ureteropelvic junction may be well delineated by roentgenography.

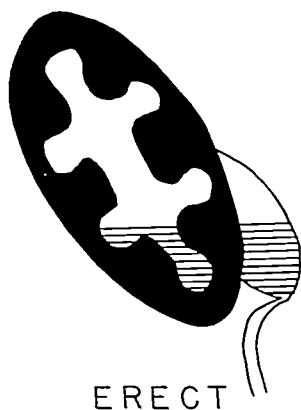


FIG 2 As in prone position, contrast medium gravitates to most dependent portion of kidney, and ureteropelvic area may be delineated by roentgenography.

of the urinary tract. Application of this principle in excretory urography to the problem of ureteropelvic obstruction is presented in figures 1 and 2.

In general, intravenous injection of 20 cc of a contrast medium containing a 35 per cent iodine compound in a patient with good renal function will be sufficient, but occasionally twice this amount may be necessary to bring into roentgenographic relief the poorly functioning, hydronephrotic kidney.

undermined to connect with the undersurface of the flaps. This permits escape of any serum that may accumulate under the flaps and no drainage material, tubes or rubber dams are necessary.

4) A complete dorsal slit is made from the base of the penis to the coronal sulcus and its edges are spread widely. This relaxing incision has a twofold purpose. It prevents any possibility of the slightest tension upon the flaps during closure and guards against any tension that might develop from edema during the early postoperative period. This incision is left open and epithelium covers this area in a surprisingly short time, usually by the end of ten days or two weeks.

5) The next step is approximation of the lateral flaps, which is accomplished by a double layer of sutures. The first layer consists of through and through silk worm gut or silver wire placed one half inch away from the edges of the skin flaps. The sutures are adjusted by use of plastic beads held in place by curved aluminum bands and so placed that when locked there is one eighth of an inch play between the two margins of the flaps. Lead perforated shots may be substituted for the plastic beads and aluminum bands. The importance of accurately adjusting the sutures should be emphasized. A suture that is drawn too tightly may cause slough at that point, the point at which this is most likely to occur is, in our experience, the penoscrotal junction. The outer layer of sutures which approximates the skin margins is of the finest possible catgut. The sutures are interrupted and inserted with care so as to prevent inversion of the skin margins. The distal ends of the flaps are brought forward and attached by mattress sutures to the glans penis so that the raw undersurface of the flap is in apposition with the denuded area on either side of the glans penis. This places the new meatus in approximately a normal position.

No dressing is required unless there is a tendency to oozing from the under surface of the flap in which case a pressure dressing may be applied for two or three hours.

The perineal urethrostomy tube is attached to a bedside bottle. The currently available antibiotics are used to prevent infection. The sutures may be removed as soon as healing appears complete, usually by the end of 10 to 12 days, and the urethrostomy tube may be removed at the same time. There may be some leakage of urine through the perineal wound during the first 24 to 48 hours but we have had no leakage after that period. The majority of these patients may be discharged from the hospital by the end of the second postoperative week.

Our experience with the Denis Browne operation has been extremely satisfactory. The scar tissue incident to the dissection on the ventral surface of the penis requires about a year to become soft and elastic. If the strip of intact skin is made of sufficient width, dilations are not necessary. The flaps have a broad base insuring an adequate blood supply and have no tendency to break down if the elementary rules of plastic surgery are observed. One of our patients had repeated bladder spasms and urinated through the newly formed canal during the first 48 hours without complicating or delaying the healing process.

In conclusion, it has been our experience that the Denis Browne operation is simple and easy to perform, is completed in one stage, requires a short period of

The excretory urographic films should be developed and interpreted separately as the series progresses. The "delayed-film," i.e., one taken at an interval later than usual in the series and in the supine position, should be studied. This may be at the 45-minute or 60-minute interval, or even later. If there appears to be good delineation of the kidney, the patient is then placed prone on the x-ray table. After ten minutes of complete rest in this position, a postero-anterior (P.A.) roentgenogram is taken. The patient is then placed supine and the table is tilted to the vertical position so that the patient is erect. Again the patient is kept completely quiet in this position for ten minutes before the roentgenogram is obtained.



FIG. 3. Excretory urogram of woman aged 20. Congenital ureteropelvic obstruction of right kidney due to intrinsic narrowing.

INTERPRETATION

One of the urographic signs commonly seen in ureteropelvic obstruction is the square or rounded, "derby hat effect" (Abowitz) of the renal pelvis. The calyces are usually proportionately dilated. Ordinarily the ureter in ureteropelvic obstruction is not visualized, or if it is, it usually appears normal dilated to the ureteropelvic junction.

Figures 3 to 5 demonstrate the effect of body position upon the location of the iodine-laden urine within the renal pelvis and calyces.

It will readily be recognized that patients with hydronephrosis due to ureteropelvic obstruction do not always have sufficient renal function to give good roentgenographic delineation of the renal pelvis. In such instances one may have to resort to retrograde study. It has been our practice to insert a No. 5 ureteral catheter approximately 4.0 cm. up the ureter on the affected side and to inject the contrast medium with the patient's body-position head down approx-

hospitalization, a factor of tremendous economic importance, and finally, is applicable to all degrees of hypospadias. For these reasons we believe it is one of the procedures of choice in the repair of this deformity.

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mately 25 degrees from the horizontal. This allows the medium to outline the ureter, and in the presence of ureteropelvic obstruction the ureter usually appears normal with very little contrast medium entering the kidney. Such a pro-

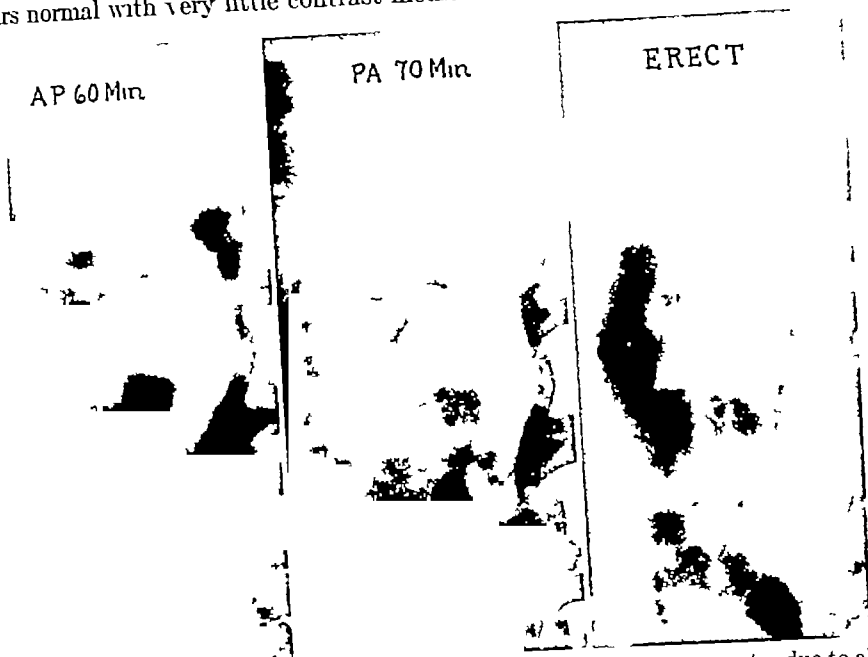


FIG 4 Excretory urogram of man aged 29. Obstruction of right upper ureter due to aberrant blood vessels.



FIG 5 Excretory urogram in erect position of man aged 23. Ureteropelvic obstruction of right kidney due to intrinsic narrowing. Note "fluid level" effect of contrast medium in middle calyx.

cedure obviates the hazard of traumatizing the ureteropelvic junction, thereby producing edema and spasm which may create an acute surgical emergency.

There may be other anatomic variations of the kidney and renal pelvis, such

MODERN TREATMENT OF HYPOSPADIAS

ARTHUR B. CECIL

The modern treatment of hypospadias has been evolved over many years. There are no operations today that have not had their roots in the past. I do not intend to discuss this subject before this association in any didactic manner, but I hope that you will permit me to discuss some phases of the treatment of this deformity. I should first like to say something in regard to the treatment of certain cases of perineal hypospadias, as these present problems not only of today but of tomorrow.

When a baby is born, who from external examination it is impossible to say whether it is a case of perineal hypospadias or female pseudohermaphroditism, we as urologists have no more ability to determine its gonadal sex than has a midwife. At no age will any cystoscopic, endoscopic or x-ray examination be of any value whatsoever, nor are there at present any chemical or biological tests for the determination of sex, but this determination must be made and made at once, unless the parents are to take home a child that will wreak as much havoc as if they had taken home a mongolian idiot. From the very moment of birth there is no place in the world for an intersex individual. The first question is, "Is it a boy, or is it a girl?" Within a few hours the State must have a report, later the Church, and make no mistake about the determination of prying neighbors to wreak vengeance on the parents of such a baby. How is this determination to be made, and when is it to be made? It must be made on the day the baby is born or within the succeeding few days according to the baby's condition by exploratory operation. Coffey, in cases of exstrophy of the bladder, successfully performed uretero-intestinal implants before the mother ever saw the child. Babies stand anesthesia well. They are accustomed to moving.

Howard has pointed out that the greater the degree of hypospadias the greater the degree of feminism, and that in practically all cases of perineal hypospadias there will be present a vagina, uterus and tubes, so that sex is not to be determined by the finding of these organs but by gonads alone. Among the problems of today and of tomorrow are to determine whether the chromosomal content of intersex individuals is normal and as to whether it corresponds with the gonadal sex.

Since I have started on the discussion of perineal hypospadias, I shall continue with this discussion to the cure of this condition. We will assume that the penis has been straightened. It has been determined by a vaginogram that the child has a vagina, and the question comes up as to what to do with this vagina. From Howard's observation that a vagina was constantly present in perineal hypospadias, it occurred to me that since I had cured many cases of perineal hypospadias without removal of the vagina, that simply because I now knew of its presence was no reason for its excision as had been previously advocated. I, therefore, constructed the urethra from the opening of the urogenital sinus.

Read at annual meeting, American Association of Genito-Urinary Surgeons, St. Louis, May 18, 1951.

as incomplete rotation, posteriorly located pelvis, and the presence of calculi, which will decrease the usefulness of the three-position technique

EXPERIENCE

From January 1945, through December 1950, we have observed 33 patients who had congenital ureteropelvic obstruction which was confirmed at operation. In each of the 33 patients excretory urography was employed.

In 7 patients retrograde urograms were obtained, and in only four of these was retrograde urography thought to be an essential part of establishing the diagnosis.

In 11 patients the three-position technique outlined in this paper was employed. This procedure was considered to be helpful in establishing the diagnosis of ureteropelvic obstruction in eight patients. The diagnosis was clear-cut roentgenographically in the delayed A P film in the remaining three patients. We did not obtain retrograde urograms in any of these 11 patients.

In the remaining 15 patients, the history, the physical examination and the routine excretory urograms were sufficient to enable us to make a correct pre-operative diagnosis of ureteropelvic obstruction.

SUMMARY

Retrograde urography in the presence of ureteropelvic obstruction carries a definite risk to the patient whereas excretory urography does not.

Urine laden with contrast medium, because of its increased density, gravitates to the most dependent portion of the urinary tract.

By obtaining excretory urograms at a delayed interval with the patient in the A P, P A, and erect positions, the ureteropelvic area can in many instances be delineated with sufficient clarity to obviate the necessity for retrograde urograms.

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to the end of the penis, thus throwing the vagina to empty into the urethra instead of excising it. I am sure that this is the best method for dealing with the vagina in cases of perineal hypospadias.

I will briefly discuss the treatment of chordee in hypospadias. This operation should be done when the child is $2\frac{1}{2}$ years old. A ventral incision is made and the fibrous corpus spongiosum is dissected out. With the penis bent back over the hand, lateral hundering bands are also dissected out. Scissors are used to free the skin laterally and up under the foreskin where right angle cuts are made to lengthen the skin. It is usually necessary to make other lateral cuts near the scrotum or any other region in which lengthening is required, but at the finish the ventral surface must be smooth without any redundancy or lumpiness of the skin. The incision is carried entirely around a No. 14 Foley catheter which has been put into the urethra. As the fibrous tissue is dissected out, the urethra moves backward, but do not cut off the cuff of the urethra as it will not leave enough urethral mucosa to easily reach the surface when healing has taken place and stricture will occur. Only spurting vessels are ligated. The urethra is sutured about with interrupted 0-0-0 plain catgut. The subcutaneous tissue and skin are closed with 0-0-0 plain catgut. If tension is present, a dorsal incision may be made without suturing. One is usually necessary at the junction of the penis with the abdomen. I have not found it necessary to suture the penis up over the abdomen. The penis is dusted with sulfamilamide powder. A pad is put over it, and adhesive tape is fastened to the thighs and brought diagonally across and another piece directly up the midline, so that the penis is in this manner strapped up over the abdomen, but the strapping must not be tight. The child will require some sedation. A $2\frac{1}{2}$ year old child can be kept reasonably comfortable with $\frac{1}{16}$ gr. of morphine every 4-6 hours and one, 1 gr. nembutal suppository at night which may be repeated. The catheter is connected with a bottle by a plastic tube. On the fourth day, the dressings are removed and the catheter is removed. There will then develop considerable edema of the penis which will subside within about three days and is of no consequence.

There are cases in which the penis is in marked ventral curvature, and in which from the region of the frenum to the urethra there is very little of the corpus spongiosum, but proximal to this, one will feel a dense fibrous corpus spongiosum running down to the region of the bulb. Just as the urethra lies below the corpus spongiosum in the ordinary case of hypospadias, so, too, in these cases, it lies below the fibrous bulb. This fibrous band must be dissected out just as if it were anterior to the urethra.

I do not believe that operations for transplanting the foreskin to the ventral surface of the penis are of value. In fact, I think they are a distinct drawback when it comes to building the urethra, nor do I believe that operations that have been devised for transplanting the foreskin to the dorsal surface of the penis are of value.

Diversion of the urinary stream is necessary for a successful urethroplasty. Culp has very successfully used a retention catheter, thus avoiding an external urethrotomy. I have previously described a method for doing external urethrotomy in hypospadias. This consists of passing a No. 16 Foley catheter through

DISCUSSION

DR W JOSEPH McMARTIN (Omaha, Neb) Drs McLaughlin and Bowler have presented a new technique which all of us can use to advantage. This interesting addition to our means of diagnosing positively ureteropelvic obstruction, in my opinion, should be used routinely in the investigation of patients with suspected pathological changes in the genito-urinary tract. The only word that might be said against this method is that in these busy times the delayed films of every patient may be annoying to the personnel of the x-ray department.

Hunner focused the attention of urologists on obstructions in the ureter. As Hugh Cabot said, "Urology owes a debt of thanks to Hunner for his extreme interest in this subject of ureteral stricture," and it seems only too true, as Legueu has said, that if the word "stricture" had not been used, but a nicer phrase such as "poor renal emptying" had been used in its stead, it would be realized that Hunner had created a clinical syndrome and had done a splendid piece of work.

It is to the urologists' credit that they have been searching for ways of avoiding the discomforts of retrograde urologic examinations when possible. We have come a long way, as is evidenced by the fact that yearly, more and more lesions of the urinary tract have been diagnosed by means of the excretory urogram. Some have claimed that every lesion in the upper urinary tract can be diagnosed by this method. Most of us, I believe, will disagree with this. Retrograde pyelography will continue to be used in most instances, but it should be used only after excretory urography has been incapable of making a definite diagnostic shadow.

It is an interesting and valuable observation of these authors that the opaque medium used in excretory urography gravitates to the caudal end of the calyceal-pelvic system when the patient is in a prone position. It is also interesting to know that in the supine position, the ureteropelvic junction normally is higher than the calyceal-pelvic system, and that when the patient is turned over on his belly, the nonopaque medium will gravitate to the ureteropelvic area, greatly enhancing the shadow at this part of the renal pelvis in ureteropelvic obstruction.

Is it true that increasing the quantity of contrast medium injected intravenously increases the chances of obtaining a satisfactory excretory urogram?

A partly damaged glomerulotubular system, such as seen in partial or early ureteropelvic obstruction, results in better elimination of the contrast medium, because the pathological changes brought about by the back pressure have rendered the semi-permeable membranes of the renal tubules more permeable.

Also, is not the real reason for the "delayed film" that, since renal excretion is 1 to 2 cc per minute, it takes renal excretory processes that long to fill a large hydronephrotic pelvis with, say, 30 to 50 cc of contrast medium and urine?

Will Dr McLaughlin, for emphasis, outline again his method of excretory pyelography, explaining the time interval between films? I think it would clarify things a good deal more.

I got this paper so late that I had little chance to try to corroborate this work,

the urethra into the bladder, and passing it in for a considerable distance so that the catheter is curled up in the bladder. Now, a straight stylet about 8 inches in length (I use a bone pin), is passed down through the catheter so that its tip within the catheter can be used to make the catheter prominent in the perineum. Having cut down upon the catheter, the stylet is used to lift the catheter into the wound, which is then grasped with a pair of forceps to keep the proximal end of the catheter from being pulled out of the bladder. The distal end is caught by a pair of forceps and pulled out through the perineal incision. To do this, it is advisable to cut off part of the funnel tip of the catheter. The object in using a straight stylet is that it is easily introduced and, what is more important, is easily removed (fig 1)

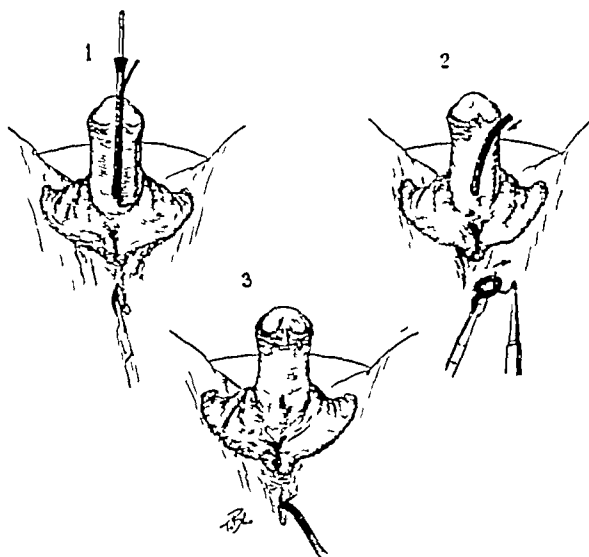


FIG 1 Cecil operation for external urethrotomy drainage

The urethroplasty is best done between 4 and 5 years of age. Like tonillectomy, children stand this operation better than older individuals. Erections do no damage to these children, but if one has to operate upon an individual beyond the age of puberty, erections are best combated by leaving nothing to chance, and every night for at least 5 or 6 nights, give HMC No. 2 or less quantity according to the age of the patient. I believe this is far more satisfactory and direct than depending upon estrogens or bromides.

There are four technical essentials for the construction of a urethra in hypospadias: 1) lack of tension, 2) a strip of undetached skin running from the hypospadias opening to the tip of the penis, 3) broad-bearing surfaces, 4) diversion of the urinary stream either by external urethrotomy or by retention catheter as advocated by Culp.

An operation which I have previously described and which has been used with uniformly good results by Cubot, Culp, Kimbrough and others, I believe most perfectly fulfills these requirements.

but I have some films of one of my patients from which Dr Vincent O'Connor kindly made some slides. I will show three slides of this patient with ureteropelvic obstruction.

(Slide) This patient has a nonfunctioning kidney on the right side, and there, as you see, is a hydroureter on her left side. You will have to take my word for it that hydroureter shows up in every film.

(Slide) This is in the same patient in the anteroposterior view, showing the increased concentration of the medium in the lower part of the pelvis, and also showing well the ureteropelvic obstruction.

(Slide) This is a retrograde ureteropelvic pyelogram of the same patient, showing, again, ureteropelvic obstruction.

STANDARD TRANSVASCULAR PROSTATIC TUMOR WITH PRIMARY GROWTH OF THE BLADDER USING OXIDIZED CELLULOSE

JOHN P. C. THOMAS JR. and GEORGE D. STUMP

From the Department of Urology, Harper Hospital, Detroit, Mich.

Suprapubic transvesical one-stage prostatectomy with primary closure is no longer showing the same transurethral resection 20 to 30 postoperative hospital days following suprapubic prostatectomy as a thing of the past. prolonged suprapubic cystostomy drainage with resultant sepsis and discomfort is inevitable. These points are adequately proved by this analysis of our first 100 cases including 15 which we published as a preliminary report.¹

The ideal transvesical prostatectomy is a one stage procedure with primary closure of the bladder wound. Modern control of hemorrhage, shock, and infection has now made this possible without the serious complications previously reported.

Lucien Lullier, who is credited with performing the first complete transurethral resection of the prostate in 1893, closed the bladder without drainage.² He kept the mortality at about 25 per cent. Trevor and England popularized the procedure in 1904 using a cystostomy tube and reported a 4 per cent mortality.

Prohman and Blodgett drainage by urethral catheter or cystostomy tube and the use of bismuth bags reduced the mortality rate to 4.2 per cent (Vivo (June 1921-26). All hospitals in 1925 averaged a mortality rate of 19.5 per cent. Brock quoted a mortality rate of 10 per cent from cystostomy alone. Hemmings and Spence were still troubled some.

Harris, von Auerswald and Fowler in America revived the idea of primary closure of the bladder in 1927. Harris' mortality rate in a large series of cases was 2.5 per cent. The risk of hemorrhage and infection prevented its widespread acceptance.

With the discovery of penicillin by Domag in 1933 and the subsequent development of antibiotics, death from sepsis became unusual. Thompson and Johnson reported the hemostatic properties of the collagen and thereby gave to prostate surgery another and toward the ideal of hemorrhage.

The one-stage prostatectomy was performed on a private patient of Dr. Weldon in February 1947. In our original report a reduction of hospital stay and postoperative discomfort was the principal achievement noted. An analysis of the results in addition to a marked reduction in postoperative mortality.

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For the sake of comparison, a series of transvesical prostatectomies and transurethral prostatectomies performed at Harper Hospital through the years 1934-37 was reviewed on the assumption that these represent the ultimate in prostate surgery before the sulfonamides and antibiotics made their appearance to help reduce postoperative complications.

A second series of transvesical prostatectomies and transurethral prostatectomies is reviewed which excludes the series of primary closure, and begins in 1946 and is carried through 1949. The review of this series was begun by Dr H. C. Jay Ellman¹ at Harper Hospital, and we have continued it. It represents prostatectomy with the supportive aid of whole blood routinely, and the prophylactic and therapeutic assistance given by the antibiotic drugs.

A comparison of these two series is given in table 1. This gives a statistical review which shows the advance made in transvesical and transurethral prostatectomy in the last 15 years in one hospital and the relative position that primary closure of the suprapubic wound occupies.

TABLE 1

1916-1937 SERIES (Thilman)		1946-1949 SERIES (Thilman)		PRIMARY CLOSURE	
Transvesical	TUR	Transvesical	TUR	Transvesical	TUR
Number of cases	23	100	229	269	100
Local hospital days (Avg.)	33	19	20	13	17
Local postoperative days (Avg.)	21	9	22	7	11
Mortality (%)	13	9	2.6	2.9	2.0
Complications					
Surgical (%)	41	30	14	28	19
Non-surgical (%)	33	11	15	6.6	5
Total	74	41	29	35	22

In total hospital and postoperative days, transvesical prostatectomy with primary closure approaches closely that of the present day transurethral prostatectomy. An interesting comparison of total hospital days may be made with a series of cases reported by Munkwitz and Seign² in which the average hospital stay was 45-50 days for both the one- and two-stage transvesical procedures. This is reduced to 35 days for our 1934-37 series to 29 days for the 1946-49 series and 17 days for the primary closure.

Of first significance is the reduction of postoperative complications in the primary closure series as compared to the previous transvesical prostatectomy series. The greatest reduction of complications occurred in the non-surgical indirect complication group. 15 per cent for the 1946-49 transvesical prostatectomy to 5 per cent for the primary closure. This may be interpreted as demonstrating the less shocking nature of the procedure postoperatively. Surgical complications were slightly higher, 11 per cent for the 1946-49 transvesical prostatectomy and 19 per cent for the primary closure.

Primary closure of the bladder had the best mortality of any group, 2 per cent.

THE EXPERIMENTAL AND CLINICAL INVESTIGATION OF VARIOUS MEDIA USED IN TRANSUMBAR AORTOGRAPHY

W F MELICK, JOHN E BYRNE and TOM D BOLER

From the Department of Urology St. Louis University and the St. Louis University Unit of the St. Louis City Hospital St. Louis Mo

In 1947 one of us presented our first years experience with translumbar aortography.¹ In 1948 we attempted to review the present status of aortography.² The possible dangers of the procedure are 1) hemorrhage from the puncture site in the aorta, 2) gut necrosis from the inadvertent injection of the medium directly into the superior mesenteric artery and 3) sensitivity reactions to the medium.

The question of bleeding from the puncture site in the aorta arose from the experimental work of Henline and Moore with dogs, in which the aortic puncture was decidedly unsafe.³ Dos Santos called attention to the fact that the arterial anatomy and physiology of the dog are not comparable to that of the human. Therefore, observations and deductions made from experimental work on dogs are valueless for a comparison of aortography on humans. No deaths have been reported in humans following translumbar aortography which have been due to hemorrhage from the puncture site. This argument has recently been reviewed in an editorial in a roentgenological journal.⁴ In this review it was also suggested from the work of Broman⁵ that the injection of high concentrations of contrast media even at great distances from the brain namely the abdominal aorta, may be the cause of cerebral damage sufficient to cause death. We believe that this is an absolutely unfounded statement. In the first place, many different investigators have published large series of cases of translumbar aortography with no deaths, the latest being Smith, Rush and Evans.⁶ In contrast to these reports, Dotter recently has reported 26 deaths in 6,824 cases of angiocardiology in the United States, Canada, Great Britain and Sweden. This vast difference in mortality alone would serve to refute any similarity between the injection of opaque medium into the aorta where it is rapidly carried to kidneys, liver, spleen, intestines and lower extremities and injection of the medium into a vein where almost all of it is then thrown into the heart and thence to the brain usually because of associated cardiovascular anomalies, the effect of which is to by-pass the pulmonary circulation.

There are now in the literature at least two reports of deaths following translumbar aortography.^{7,8} We also have knowledge of several other deaths through

Read at annual meeting American Urological Association Chicago Ill May 24 1951

¹ Vitt A E and Melick W F J Mo State Medical Assoc 44 749 1947

² Melick W F and Vitt A E J Urol 60 321 1948

³ Henline R B and Moore S W Am J Surg 32 222 1936

⁴ Editorial Am J Roentgenol & Rad Therapy 65 280, 1951

⁵ Broman T Forssman B and Olsson O Acta Radiol 34 135 1950

⁶ Smith P G Rush T W and Evans A T J Urol 65 911, 1951, also 66 145, 1951

⁷ Dotter C T and Jackson F S Radiology 54 527 1950

⁸ Wagner F B and Price A H Surgery 37 621 1950

⁹ Sante, L. Radiology, 56 183 1951

group of control mice were used in conjunction with each series of extracts assayed

In every instance, the uterine weights within each group of mice associated with a particular specimen were averaged, and the same procedure was followed with the control mice. An increase of 100 per cent in weight over the average weight of the unstimulated control uterus was taken as our mouse uterine unit. With this as the standard, and by using the proper factor determined by averaging each specimen into equal fractions for each mouse in a group, gonadotrophins were calculated in mouse uterine units for each specimen.

In a few of the assays, several of the mice died as noted in figures 1, 2, and 3. M.D. No results were recorded for these specimens.

The results were placed on a separate graph for each subject. In illustration, the graphs of four of the 6 subjects are shown in figures 1-3. Figures 1-3 are the graphs of Subjects I-III respectively. Subject V. The height of each graphic column represents the average uterine weight for that particular day, measured in mouse uterine units. The fractional results (figures 1, A-3, A corresponding to Subject V) are illustrated except that each is represented by a vertical column for each day. This demonstrates the additive effect of each column represents the first specimen for that day, et cetera. For clarification, the 6 hour fractional specimens, numbered 1-6, are illustrated separately in succession. This allows comparison of the results of the fractions. Days in which ejaculation occurred are marked by heavy black arrows. Numbers on the graphs. Occurrence of ejaculation during the period is marked directly by a heavy black arrow.

During the course of the bioassays, individual specimens were recorded on all subjects to accepted standards, were recorded on all subjects.

RESULTS

In the analysis of the work outlined in this paper, the terms "negative response" were arbitrarily adopted. A positive response was one in which the gonadotrophin titer on the day of collection was higher than the average of the day before and the day after collection. A negative response was the reverse, i.e., a lower titer on the day of collection than the average of the day before and the day after. Obviously this applies to situations where the mice died, urine was not collected, or ejaculation occurred on successive days. The response was not included in these determinations. In acceptable situations, twenty showed positive response.

The following is a brief summary of the essential features of each subject and a short discussion of the results.

Subject I, 35 years old, married, proven fertility, no known disease. Urine was collected for 23 days. During the collection period, ejaculation was timed with the start of the fifth six hr.

personal communications with other investigators although these have not yet been reported. In all of these cases death has been the result of the necrotizing effect of sodium iodide on the intestine when it has been inadvertently injected into the superior mesenteric artery. Because of these deaths, Wagner and Price⁹ have suggested a preliminary injection of 10 cc of 30 per cent sodium iodide into the aorta and an x-ray taken to be sure the needle is not in the superior mesenteric before proceeding. If a less necrotizing medium than sodium iodide can be found these precautions can be omitted without fear of fatality. A recent article in the British literature¹⁰ suggests the use of 70 per cent diodone as a medium instead of sodium iodide to avoid possible complications. We too have long recognized the inherent dangers in the use of sodium iodide and last year before the South

TABLE 1

COMPOUND	PERCENT IODINE
Sodium iodine	84.7
Urokon	65.5
Neo-iopax	51.5
Diodrast	49.8



FIG. 1. Seventy per cent diodrast, 70 per cent urokon, 75 per cent neo iopax and 80 per cent sodium iodide placed in same sized tubes. X-ray made at 36 inches 0.2 second, 40 ma, 70 k.v. Order of density, sodium iodide most opaque, followed in order by urokon, neo iopax and diodrast.

Central Section described the use of 75 per cent neo-iopax as a possible substitute though not an entirely satisfactory one.¹¹

Our anesthetists have called to our attention that during and following the injection of 80 per cent sodium iodide, and to a lesser extent following 75 per cent neo-iopax, the anesthetized patient shows some cyanosis and a speeding up of pulse rate. Also, if the patient is not in complete surgical anesthesia, he exhibits signs of severe pain when the sodium iodide or neo-iopax hits the aorta. When the Mallinckrodt Chemical Works released urokon sodium, and its use in excretory urography proved so innocuous, its application in higher concentrations as a medium for aortography occurred to us. As soon as a 70 per cent solution was developed, Dr. M. A. Thorpe of the Mallinckrodt Chemical Works released com-

¹⁰ Griffiths, I. H. Brit. J. Urol., 22: 251, 1951.

¹¹ Melick, W. F., Yarbrough, C. P. and Boler, T. D. J. Urol., 65: 455, 1951.

According to definition, five positive responses occurred as opposed to one negative response. These acceptable response periods were days 1-3, 3-5, 7-9, 12-14, 15-17, and 21-23. A significant variation in gonadotrophin titer was obtained during the three day fractional period. It is of interest to note that the highest titers occurred during the third and fourth periods (12 to 24 hours) after ejaculation. Comparatively this is a slightly delayed elevation following ejaculation.

Subject II, 28 years old, married, proven fertility, normal semen specimen

There were two periods of urine collection, the first series for seventeen days, and the second series for nine days. On the seventh day of the first series and the fourth day of the second series, the extracts were toxic enough to kill the mice

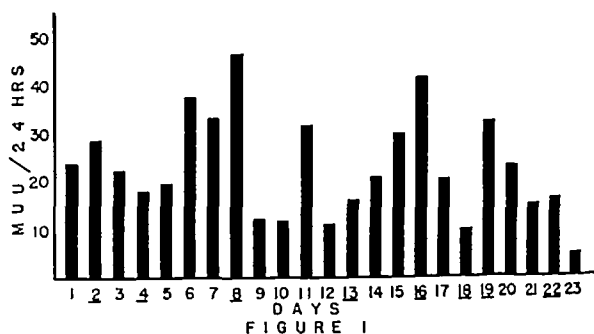


FIGURE 1

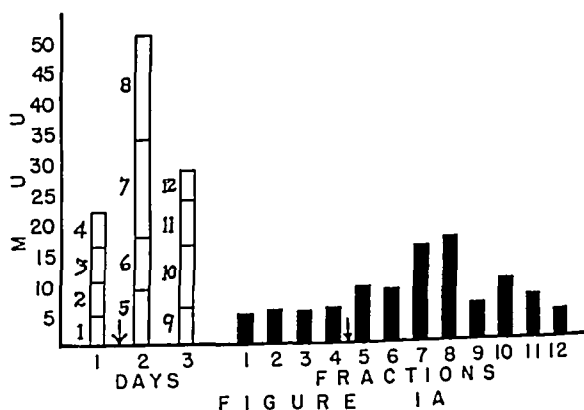


FIGURE 1A

Ejaculation was scheduled at the start of the three days of fractional collections. See figure 2.

Three acceptable responses were exhibited, all positive. These are noted at days 8-10 and 15-17 of the first series, and days 7-9 of the second. All of them were marked and definite. In addition, ejaculation also coincided with days 1 and 2 of the first series, and day 1 of the second. Although by definition there are not response situations, it is interesting to note that the titers on these days were higher than the titers for any non-ejaculatory day and much higher than the non-ejaculatory day average for the particular series. With ejaculation occurring at the onset of the fractional collecting period, by far the largest graphic block is that for the first six hours. This indicates an immediate type of response.

for animal experimentation Urokon is an organic iodine compound, but sensitivity reactions have been far less frequent and less severe than compounds used heretofore. A survey in our city has shown only one hospital which has had any evidence of a sensitivity reaction to urokon when used for excretory urography, out of thousands of cases which have been done.

In a recent paper on the use of subcutaneous organic iodine compounds to secure excretory urograms on infants, two of us have reported on the effect of the various media on the subcutaneous tissues of guinea pigs.¹² At that time we

TABLE 2 Guinea pig reaction to intramuscular and subcutaneous injection of 200 mg per kg of opaque media and hyaluronidase*

ANIMAL	MEDIA	GROSS REACTION	MUSCLE	SUBCUTANEOUS TISSUES	KIDNEY
1	Neo iopax 50%	0	0-1	0	0
2	Neo-iopax 75%	0	2-3	0	0
3	Urokon 70%	0	0-1	0	0
4	Urokon 30%	0	0	0	0
5	Diodrast 70%	Local necrosis	2-3	2-3	0
6	Diodrast compound	0	2-3	2-3	0
7	Sodium iodide 70%	Local necrosis	3-4	1-2	Tubular necrosis
8	Aldase and saline (control)	0	0-1	0	0

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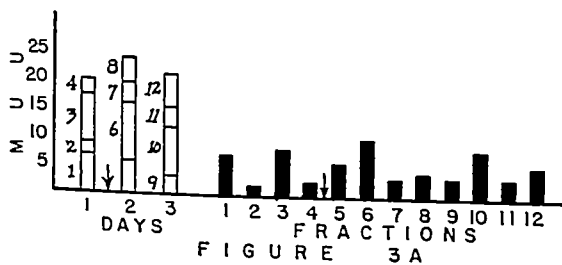
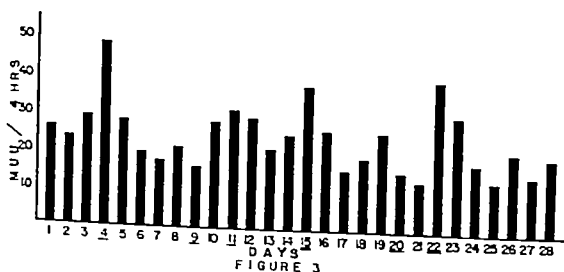
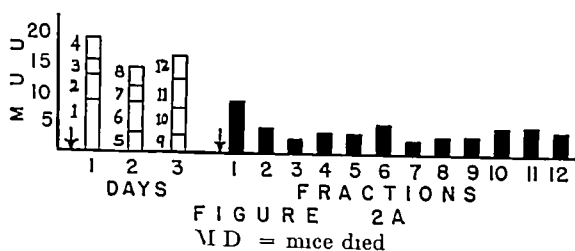
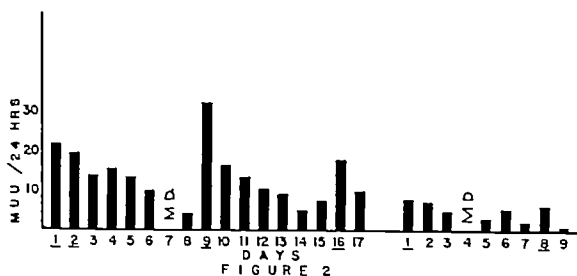
TABLE 3 Effect of media injected directly into superior mesenteric artery of dogs (20 cc used in each case)

DOG	MEDIUM	0-5 MIN.	15 MIN.	FINAL OUTCOME
1	Na I 80%	Marked hemorrhage and spasm	Spasm hemorrhage, cyanosis	Death from gut necrosis
2 and 5	Diodrast 70%	Moderate spasm and cyanosis	Cyanosis and spasm better, petechial hemorrhages	Recovered
3 and 6	Urokon 70%	Mild spasm and cyanosis	Cyanosis and spasm gone, petechial hemorrhages	Recovered
4 and 7	Neo-iopax 75%	Moderate spasm and cyanosis	Cyanosis and spasm better, petechial hemorrhages	Recovered

used the media available for aortography, namely sodium iodide, 70 per cent diodrast, 75 per cent neo-iopax, and 70 per cent urokon. The relative iodine content of these are listed in table 1. The comparative x-ray densities are shown in fig 1 where each of the media was placed in the same diameter test tube and an x-ray exposure made. Sodium iodide as expected from the iodine content is the most dense, followed in order by 70 per cent urokon, 75 per cent neo-iopax, and 70 per cent diodrast.

¹² Byrne J E and Melick, W F. Subcutaneous urography. Description of a new method utilizing 70% urokon and hyaluronidase. A preliminary report. *Urol & Cutan Rev In press*

Subject III, 35 years old, married, seven year sterility problem culminating finally in pregnancy with full term normal delivery The semen analysis showed a count of only 5,000,000 per cubic centimeter and a total count of 25,000,000 The specimen was essentially normal in all other respects



Urine was collected for 28 days. Two ejaculations occurred during the fifteenth 24 hour period of collection. The first ejaculation was recorded during the first six hours of collection and the second occurred three hours before the end of that 24 hour collection. Ejaculation during the fractional collections fell just at the start of the fifth specimen collection, i.e., at 24 hours. See figure 3.

The reaction of these in muscle and subcutaneous tissue and the effect on the kidney are shown in table 2

From this study it appears that the body tissues react less to urokon and neo-iopax than to diodrast and diodiast compound. All of the organic iodine compounds, however, are better than sodium iodide.



FIG 2 A, one of series of serial pictures made as 20 cc of 80 per cent sodium iodide was injected into occluded aorta of dog. Note dye filling loops of intestine. B, later picture in same series. Loops of intestine now filled with sodium iodide. Dog died of gut necrosis and aortic hemorrhage.

TABLE 4 *Effect of media instilled into occluded aorta so that dispersion of dye is almost completely into gut (20 cc dye used for each)*

DOG	MEDIA	0-5 MIN	10 MIN	OUTCOME
1	Urokon 70%	Mild spasm and slight cyanosis	Recovery	Gut normal, death from aortic hemorrhage
2	Neo-iopax 75%	Mild spasm and slight cyanosis	Recovery	Living
3	Diodrast 70%	Mild spasm and slight cyanosis	Recovery	Living
4	NaI 80%	Hemorrhage, cyanosis, spasm	Hemorrhages, spasm, cyanosis deeper	Death from hemorrhage and gut necrosis

Results parallel those of previous experiments (table 3). Less reaction noted, because of lack of direct trauma to superior mesenteric artery.

Seven adult dogs were then used to determine the effect of the injection of 20 cc of the various media directly into the superior mesenteric artery. At this time let us reiterate again that the findings of Henline and Moore are correct concerning bleeding from needle puncture wounds in the aorta of dogs. In our series, several dogs were lost through hemorrhage from the aorta following injection through small needle punctures. The present experiments were run solely to

Four positive and two negative responses were recorded. The former occurred on days 3-5, 10-12, 14-16, and 21-23, and the latter on 8-10 and 19-21. In the 14-16 day group, ejaculation occurred twice, as previously noted, but the result is not significantly different from any other positive response. The fractional period graph shows the largest titer in the sixth block, or the second six hours following ejaculation, indicating an early response. The combined titer of the fifth and sixth blocks is greater than that of the combined titer of any two other consecutive blocks in the three days.

Subject IV (not illustrated), 26 years old, married, proven fertility, normal semen specimen.

Urines were collected for 28 days. Three positive and one negative responses were noted. It was of interest to note that during the collection period, ejaculation occurred on the second and third (two successive) days. The average titer for

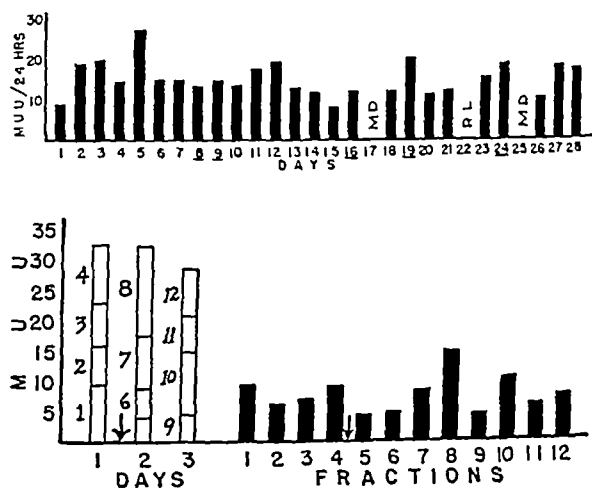


FIG 4

M D = mice died
R L = residue lost

these two days was more than twice the average titer for the first and fourth days. The three day fractional graph revealed a definite response spread more or less evenly over the four six hour periods immediately following ejaculation. Comparatively this indicates a slightly delayed response.

Subject V, 28 years old, single, semen specimen showed a count of 30,000,000 per cubic centimeter but a total of 150,000,000 with all other elements within normal limits.

Urine was collected over 28 days. During the collection of fractional specimen, ejaculation was timed with the start of the fifth six hour period. See figure 1.

Only one acceptable situation was noted, days 18-20, and this was a definitely positive response. Three situations that would have been acceptable were not recorded because of the premature death of the mice associated with two critical specimens and the inadvertent loss of the residue of a third specimen. In this case also, there was a four day period during which ejaculation occurred during the

determine the toxicity of the various available media when injected directly into the superior mesenteric artery. The same technique was used in all cases. A midline abdominal incision was made under intravenous or intra-arterial anesthesia with veterinarian nembutal. The superior mesenteric artery was exposed and then injected with a No. 21 needle as rapidly as possible. The results are tabulated in table 3.

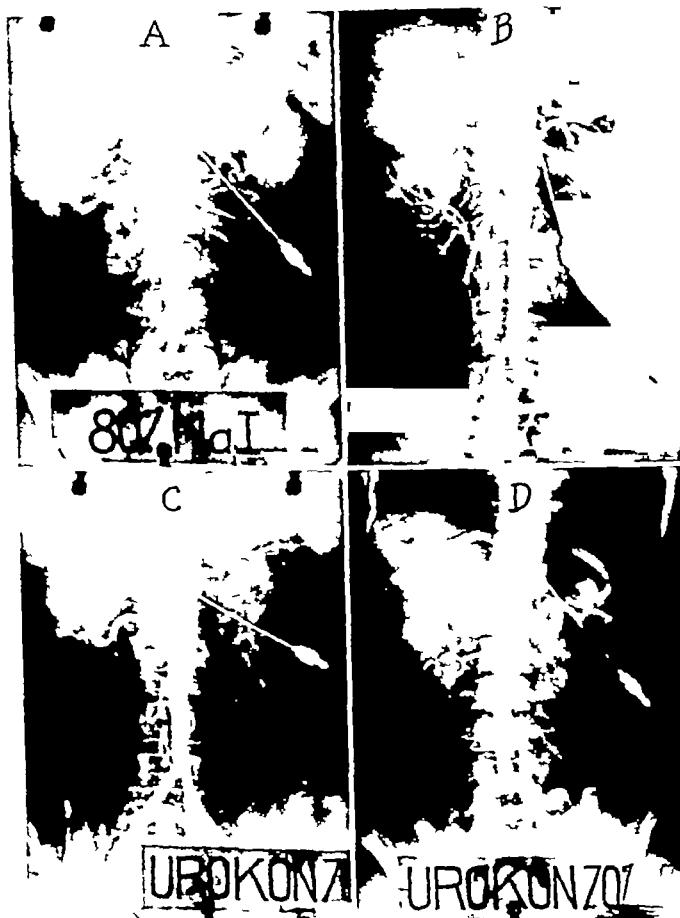


FIG 3. *A* normal aortogram made with 80 per cent sodium iodide. Compare with *C* and also figure 4. *B* aortogram made with 80 per cent sodium iodide simulates left cyst actually proved to be hydronephrosis. *C* normal aortogram made with 70 per cent urokon. Compare with 4 and also figure 4. *D*, aortogram in horseshoe kidney. Note absence of major vessels in isthmus. 70 per cent urokon.

A very valid objection to this procedure is the possibility of the effects being due to trauma of the artery by the needle puncture with subsequent ischemia of the gut. In dogs the superior mesenteric artery is small in caliber. A second series of 4 dogs was done by occluding the aorta just below the superior mesenteric artery and instilling the medium into the aorta just above the origin of the mesenteric artery. During this procedure with sodium iodide a series of serial

middle two days, days 7-10. However, in contrast to the previous case (IV), the gonadotrophic response was almost identical for all four days without any elevation associated with ejaculation. This poor type of response was noted, comparatively speaking, throughout the entire collecting period regardless of when ejaculation occurred. This observation was also strengthened by the titers noted in the three day fractional period. Although actually a titer change was demonstrated, the additive results of the first and second days were almost the same, in spite of the occurrence of ejaculation exactly between these days. The third day titer was only slightly lower. This represents a poor gonadotrophin response to the stimulus of ejaculation.

Subject VI (not illustrated), 28 years old, single, normal semen specimen

Urines were collected for 28 days. Four applicable responses were demonstrated, all positive. However, the highest titer recorded in this subject was that of day 28, which was not associated with ejaculation. Coincident with this high titer the subject had developed a moderately severe streptococcal tonsillitis and pharyngitis with a concomitant fever of 103°F. Because of the remarkably high titer obtained for day one, much greater than that of either days 2 or 3, the three day fractional studies in this subject were not significant.

DISCUSSION

In contrast to the extensive gonadotrophin studies conducted for many years in women of all ages, and man in abnormal circumstances and old age, records of continuous gonadotrophin excretion by the normal human male have been of comparatively recent origin. Daily variations in the titer have been noted only incidentally. As for a physiological explanation of these changes, none has been recorded.

Separation of the gonadotrophin components excreted in the urine has not been accomplished. The combined effects of the total gonadotrophin excretion are measured in bioassay techniques employed in this paper. In a series of experiments with immature and/or hypophysectomized animals, conclusive observations on the presence of multiple gonadotrophic components in the normal human male urine have been established.^{2,7} This work has led to the surmise⁸ that

² Greep, R. O., van Dyke, H. B. and Chow, B. F. Separation in nearly pure form of luteinizing (interstitial cell stimulating) and follicle stimulating (gametogenic) hormones of the pituitary glands. *J. Biol. Chem.*, **133**, 289-290, 1940.

⁷ Greep, R. O., van Dyke, H. B. and Chow, B. F. Gonadotrophins of swine pituitary, various biological effects of purified thylenkentrin (FSH) and pure metakentrin (ICSH). *Endocrinology*, **30**, 635-649, 1942.

⁸ Fraenkel Conrat, H. L., Li, C. H., Simpson, M. E. and Evans, H. M. Duality of pituitary gonadotrophins. Effects of FSH-ICSH mixture on hypophysectomized male and female rats. *Proc. Soc. Exper. Biol. and Med.*, **48**, 723-726, 1941.

¹ Fevold, H. L. The gonadotrophic function of the pituitary gland, from *The Chemistry and Physiology of Hormones*, ed. by Moulton, F. R., Lancaster, Pa., The Science Press Printing Co., 1944, ed. 1, p. 153.

¹ Leatham, J. H. and Levin, L. Gonadotrophic action of normal male urine extract on ovaries of normal and hypophysectomized immature rats and of immature mice. *Endocrinol.*, **29**, 8-17, 1941.

Hildebrand, A. G. and Riney, E. H. Review of the literature on the pituitary gland (1940 and 1941). *Arch. Int. Med.*, **71**, 262-296, 1943.

¹ Heller, C. G. and Nelson, W. O. The testis-pituitary relationship in man. *Recent Progr. Hormone Research*, **3**, 229-255, 1948.

pictures was made (fig 2) according to our previously reported technique.¹¹ The serial aortograms show conclusively that the injected medium is thrown into the intestines. Where sodium iodide was used, the dog died of gut necrosis similar to the human deaths reported in the literature. In the cases of the organic iodine compounds, there was some initial reaction but no deaths from gut necrosis. It would seem that these are clinically safe even if inadvertently injected directly into the superior mesenteric artery. The results of these experiments are shown in table 4.

CLINICAL USE

Because of its lower tissue reaction, greater iodine content and hence greater x-ray density, and failure to produce gut necrosis even when injected directly into the superior mesenteric artery of dogs, 70 per cent urokon was thought to be worthy of a trial in the human. Our results to date have been most encourag-



FIG 4 Normal aortogram made with 75 per cent neo iopax. Detail in smaller vessels does not stand out as well as sodium iodide or urokon (fig 3, 1 and C).

ing. While we have been fortunate in not injecting it directly into the superior mesenteric artery, there has been no evidence of toxicity or reaction in the anesthetized patient when 70 per cent urokon was used. Our anesthetists were the first to point out its marked superiority in this respect.

The only change in our previously published technique has been the use of hand injection and an increase in volume of the injected medium to as much as 25 cc. For purpose of comparison, aortograms made with 80 per cent sodium iodide, 70 per cent urokon and 75 per cent neo-iopax are reproduced in figures 3 and 4. Neo-iopax does not give as satisfactory a picture as does urokon. We believe the 70 per cent urokon gives a picture which is suitable for diagnosis.

After 25 cases of translumbar aortography with 70 per cent urokon had been done, we then tried the procedure on 10 patients under local anesthesia. The patient is prepared in routine fashion and given any desired preoperative sedation, either demerol and hyoscine or morphine and hyoscine. The skin is incised

the male urine normally contains large amounts of follicle stimulating hormone, detectable amounts of interstitial cell stimulating hormone (luteinizing hormone), and unknown amounts of a third gonadotrophin called luteotrophin

Prior to the experiment discussed in this paper, work on the male has demonstrated no comparable approach to the well illustrated female cycle variations.¹² Earlier research on normal male urinary gonadotrophins centered on quantitative techniques.¹⁴⁻¹⁶ Titer fluctuation was not described. Levin's observations of titer fluctuations in 1941¹⁷ led him to conclude that these daily changes in each male have no significance. Heller, et al.¹⁸ noted marked variations in the gonadotrophin titers of adult human males. However, it was felt that the male excretion rate is erratic over a wide range. Errors in technique and difference in animal response were presumed to account for some of the disparity. Finally, they concluded that a trend towards a periodic cyclic increase or decrease in titer level could not be shown in their cases.

Basically this paper centers on the dynamic interrelationship of the hypophysis and the testis. In the words of Hamilton,¹⁹ "Both functions of the testis, spermatogenic and endocrinous, are induced by, and dependent for maintenance on, gonadotrophins from the anterior lobe of the pituitary." Apparent control of seasonal testicular activity in animals by the anterior pituitary has been described.²⁰⁻²¹ Both of these animals studies reveal comparable similarities to the situation suggested in this paper regarding the association of elevated gonadotrophin levels with spermatogenesis.

Observations of changes in gonadotrophin level in man at the time of puberty, prior to which spermatogenesis does not occur, also lend strong support to the physiological significance of the results of this experiment.*

⁹ D'Amour, F. L. and Woods, L. The sex cycle of a normal woman. *J Clin Endocrinol* **1**: 433-435, 1941

¹⁰ von Ham, E. and Rothermich, N. O. Excretion of gonadotrophic and estrogenic hormones in urine during normal menstrual cycle. *Proc Soc Exper Biol and Med*, **44**: 61-371, 1940

¹¹ D'Amour, F. L., Funk, D., and Liveman, H. Daily gonadotrophic hormone tests during 50 complete menstrual cycles. *Am J Obst and Gynec*, **37**: 940-946, 1939

¹² Heller, I. J. Gonadotrophic hormone. Urine assays during the menstrual cycle in normal women. *J Clin Endocrinol*, **1**: 813-820, 1941

¹³ D'Amour, F. L. A qualitative study of normal gonadotropin. *Am J Physiol*, **127**: 649-653, 1939

¹⁴ Katzman, P. A. The quantitative determination of the gonadotropic material of the urine of women after castration and the menopause and of normal men. *Endocrinol*, **21**: 89-95, 1937

¹⁵ Levin, L. and Tyndale, H. H. The quantitative assay of follicle stimulating substances. *Endocrinol*, **21**: 619-628, 1938

¹⁶ McCullagh, D. R. and Bowman, W. E. The extraction and assay of gonadotropic hormones from human male urine. *Endocrinol*, **27**: 525-526, 1940

¹⁷ Levin, L. Quantitative precipitation of urinary gonadotropin of normal men and women. *Endocrinol*, **28**: 375-387, 1941

¹⁸ Heller, I. J., Heller, C. G. and Sevrinhaus, L. L. Gonadotropic hormone, assay of human male urine. *Endocrinol*, **29**: 1-7, 1941

¹⁹ Hamilton, J. B. The therapeutics of testicular dysfunction. *JAMA*, **116**: 1445-1446, 1941

²⁰ Moore, C. R. The physiology of the testis. *JAMA*, **116**: 1638-1644, 1941

²¹ Wells, I. J. Seasonal sexual rhythm in the male of 13-lined ground squirrel. *Am J Zool*, **62**: 409-417, 1935

Katzman, P. A. and Doisy, E. A. A quantitative procedure for determining normal excretion of prolactin. *Proc Soc of Exper Biol and Med*, **30**: 1188-1191, 1933

²² Klinefelter, H. F., Jr., Reifenstein, J. C. and Albright, F. Syndrome characterized by

thetized by injection of 1 per cent novocain and a paravertebral block carried out in routine fashion. The needle for aortography is then inserted into the aorta. A definite sticking sensation is felt by the patient when the aorta is entered. The 70 per cent urokon is then injected in routine fashion using a 20 cc Luer lock syringe and hand pressure. The patient usually experiences a moderate cramping sensation at this point. Immediately following the injection there is also some nausea and infrequently vomiting. This reaction has been noted in intravenous pyelography with urokon where the dye is injected rapidly.^{13 14} In no case has this been a serious problem. We believe that this is the first series of translumbar aortography which has been done under local anesthesia.

SUMMARY

The possible dangers of translumbar aortography have been reviewed, only one of which, namely gut necrosis due to irritation of sodium iodide, has led to any reported deaths.

The relative x-ray densities of available media have been listed.

The local reactions of the various media when injected into the superior mesenteric artery of the dog have been described.

The successful use of a new product, urokon sodium 70 per cent has been reported as the opaque medium in translumbar aortography. We believe that it more nearly approaches an ideal medium for translumbar aortography than anything else available.

Using urokon sodium 70 per cent, translumbar aortography has also been possible under local anesthesia.

The solution of urokon sodium 70 per cent used in the experimental and clinical studies was supplied by Dr. M. A. Thorpe of the Mallinckrodt Chemical Works.

539 N. Grand Ave (W. F. M.), 6420 Clayton Rd (J. E. B.), 1515 Lafayette Ave (T. D. B.), St. Louis, Mo.

¹³ Nesbit, R. M. and Lapidus, J. J. *Urol.*, **63**, 1109, 1950.

¹⁴ Richardson, J. F. and Rose, D. K. *J. Urol.* **63**, 1113, 1950.

Although for simplicity the actual discussion of the results of this experiment was included in the previous section, it is of further interest to compare the results recorded in subjects III and V. Both, by accepted standards, had low spermatozoal counts, 5,000,000 and 30,000,000 per cc respectively, although the total count for the latter was 150,000,000. The former subject, III, has a heavy beard and comparatively harsh voice while the latter has a light beard and comparatively soft voice. Subject III follows athletics very closely, participates actively in sports and has a heavy muscular build. In contrast, Subject V is nonathletic, neither following nor participating actively in sports, and has a light build. Finally, a relatively dynamic forceful personality characterizes the former, while a shy, comparatively retiring personality can be ascribed to the latter. A testicular biopsy, taken in the course of a sterility workup on subject III, revealed a moderately advanced interstitial fibrosis. These two individuals were chosen purposely as subjects in this experiment because of their common low sperm counts per unit volume and their drastically divergent general characteristics.

Comparing the graphs of each of these two subjects over the 28 day collection periods, III showed a markedly higher average daily titer than did V. Also, in spite of two negative responses in subject III, the general picture was one of definite response, while in subject V, with one exception, there was little demonstrable change in titer level regardless of the occurrence of ejaculation. The suggested implication is obvious. The inadequacy demonstrated by subject III lies in a deficient testicular germinal epithelium in the presence of a normally functioning anterior pituitary, while in subject V, the anterior pituitary may be mildly insufficient in gonadotrophic elaboration with a resultant secondary effect on the testes as part of the picture.

A few instances of unexplained high titers were obvious in the overall results. These occurred in non-ejaculation phases. One of these elevations, a particularly high level, occurred as already noted in subject VI in association with a moderately toxic state. It is a known fact that in febrile states the general body metabolism is increased correspondingly. It is only logical to assume, therefore, that the pituitary metabolic processes, as part of the general picture, are also stepped up. This would result in increased hormone production, including the gonadotrophic components, by the pituitary. Perhaps there are other conditions, somatic or emotional which exert influence on pituitary activity and thereby incidentally increase the urinary gonadotrophin titer.

Gynecomastia aspermatogenesis without Leydigism and increased excretion of follicle-stimulating hormone. *J Clin Endocrinol* 2 615-627 1942

Heller C G and Nelson W O. Hyalinization of seminiferous tubules associated with normal or failing Leydig-cell function: discussion of relationship to eunuchoidism, gynecomastia, elevated gonadotrophins, depressed 17 ketosteroids and estrogens. *J Clin Endocrinol* 5 1-12 1945a

Heller, C G and Nelson W O. Hyalinization of seminiferous tubules and clumping of Leydig cells: notes on treatment of clinical syndrome with testosterone propionate methyl testosterone and testosterone pellets. *J Clin Endocrinol* 5 27-33 1945b

Nelson W L and Heller C G. Hyalinization of seminiferous tubules associated with normal or failing Leydig-cell function: microscopic picture in testis and associated changes in breast. *J Clin Endocrinol* 5 13-26 1945

Reutenstein E C Jr. Hereditary familial hypogonadism. *Proc Am Federation Clin Pearch* (1946) 3 86 1947

DISCUSSION

DR PARKE G SMITH (Miami, Fla) As you may know, we for sometime have been keenly interested in what, as urologists, we choose to call "renal arteriography" as accomplished by the translumbar route Dr Melick's report is added evidence of the correctness of the contention that renal arteriography when performed in a simple but precise manner, using a nonnecrotizing contrast medium is one that is safe and is available to all urologists

I was particularly interested in Dr Melick's discussion of what previously has been regarded as the dangers of aortography, namely damage to the aorta as the result of the puncture and the toxic or necrotizing effect of the contrast media injected

We have previously reported to this Association the result of a post mortem study of the aortas of 13 moribund patients, whose aortas were punctured immediately before death, and a similar study of the aortas of 9 patients who died from nonrelated causes several weeks after aortic puncture In none of these cases was there evidence of damage to the aorta, even though these patients for the most part were extremely old, had sclerotic arteries and frequently large atheromatous plaques in the aorta Since the time of that report that study has been increased in scope, but as yet we have found no evidence of damage that could be attributed to the puncture itself, or evidence of peri-aortic hemorrhage of clinical importance We are indeed happy that the essayist agrees that the supposed danger of aortic puncture is one that is nonexistent

We have had no experience with the use of sodium iodide Our efforts have been confined entirely to the use of the nonnecrotizing solutions, but we have limited the quantity of the solution injected to a point below that which is usually regarded as being a toxic amount It is seldom that we use more than 14 cc of the contrast medium

We have had the opportunity of using all three of the nonnecrotizing solutions referred to by Dr Melick That the use of such a solution in the small amounts referred to above and according to a simple precise technique previously reported by us, is safe is attested by the fact that our group now has a personal series of well over seven hundred renal arteriograms performed by the translumbar route without mortality or morbidity of more than a few hours

The essayist stated that as yet he had not had the misfortune to inject directly into the superior mesenteric We had had that accident on two or three occasions but we have observed no complications as a result of that accident I should like to show you a film of one of these cases You can see that the injection has actually reached the point of visualizing the small branches of the wall of the descending colon, yet this patient did not even have diarrhea We have accidentally injected practically everything in this area in which there is arterial blood without any embarrassing complications to us or the patient

I should like to show you another film that was made very recently, which shows a beautiful demonstration of the injection of the arterial supply of the liver, spleen and the pancreas This patient had absolutely no difficulty and a satisfactory renal arteriogram was made the following day All of the films you have just seen were made with 14 cc of neo-ropin

In review, excluding the fractional periods, 24 acceptable responses are recorded. Of these, 20 are positive and four are negative, according to the arbitrary definition previously proposed. Determining the statistical significance of the results obtained in this experiment presents certain difficulties. The authors feel that a simple calculation, definitely suggestive of statistical significance, is all that is warranted. Very roughly, it has been determined that the probability of 20 positive responses, not in succession or in any order, occurring in a total of 24 measurable responses purely by chance is approximately one in 2,000.*

CONCLUSIONS

The results obtained in these observations on six adult males suggest that the act of ejaculation may be a specific initial stimulus in a chain of normally occurring reactions. These physiological changes result in increased production and/or elaboration of gonadotrophin by the anterior pituitary as measured by urinary gonadotrophin levels.

It is also suggested that the response of the anterior pituitary to the initial stimulus of ejaculation is apparently rapid, generally occurring within 24 hours of ejaculation. This period of activity is in turn followed by one of comparatively quiescent gonadotrophin production as measured by urinary gonadotrophin excretion.

The possibility must be entertained that the pituitary gonadotrophin response may be subject to influences other than the act of ejaculation. General changes in body metabolism, normal or abnormal, psychic or physical, that incidentally affect the anterior pituitary as a whole, may be responsible for a transitory increase in gonadotrophin titers.

Finally, with merely two subjects of widely variant natural characteristics for comparison, it is pointed out that an abnormal semen specimen may or may not be associated with an atypical gonadotrophin response to ejaculation.

SUMMARY

Urinary gonadotrophin excretion titers in six adult male physicians were measured over extended periods of time.

An attempt to associate physiological significance with gonadotrophin titer variation has been made.

A correlation between gonadotrophin titer rise and ejaculation time in the male is suggested.

Extraneous causes of male gonadotrophin titer variations are suggested.

* The equation $\sigma = \sqrt{npq}$ is employed (28), where σ is the standard error of simple sampling, n is the total number of responses, p is the probability of one response being positive by chance alone, and q is the probability of one response being negative by chance alone. The actual probability is then obtained by the fraction, $\frac{x}{\sigma}$ where x is the difference between the number of positive responses and half the total responses, assuming that by chance alone there would be the same probability of any one response being either positive or negative.

† Pearl, R. Medical Biometry and Statistics. Philadelphia: W. B. Saunders Co. Paper 3, pp. 317 and 320.

I should like to speak briefly about the comparative values of the three solutions referred to by Dr Melick as shown by our experience. We wish to emphasize that as yet none of them is completely satisfactory, particularly in so far as their contrast ability is concerned, but we believe that their shortcomings in that respect can at least in part be eliminated by developing precision in your technique.

Diodrast has been used very rarely and I am not prepared to form any opinion as to its precise values.

We have used 75 per cent neo-iopax extensively and have found it to be as satisfactory as any of the solutions now available. Last year during the meeting of this Association held in Washington, D. C., Dr Thorpe of the Mallinckrodt Chemical Works asked if we would be interested in investigating the use of urokon in renal arteriography. We expressed not only willingness, but our pleasure in having the opportunity of doing so. We told him that we felt this solution should be at least 70 per cent, which was a more concentrated solution than they as yet had made. Shortly after that time he furnished us with 200 ampules of the solution.

In order to avoid toxic effects, as already mentioned, we use only a small quantity of the contrast medium. It follows that the time of the one-tenth of a second exposure that we use is a matter of extreme precision. Unfortunately, during the first few cases in which we used 70 per cent urokon the patient, even though under intravenous anesthesia, gave a gasping sigh just at the time the exposure was to be made. We became discouraged and I must admit we may possibly have been too greatly impressed by the previously reported necessity of injected urokon slowly when doing excretory urography. I believe Dr Melick has referred to that fact.

We therefore discontinued the use of this solution for several months and it was not until about the first of this year that we again began using it. Since that time we have made approximately seventy arteriograms with urokon. We have a small series of 11 patients who have had arteriograms made on two consecutive days, one with neo-iopax and one with urokon. We are unable to see any particular difference in the contrast value of these two solutions and when we have found a better arteriogram with one than with the other we have felt it was due to precision of technique rather than to the contrast character of the solution used.

As our experience with urokon has increased, we are not as greatly impressed with the likelihood of gastric irritability as we were initially, but we still believe that the tendency toward this undesirable effect is somewhat more marked in urokon than the other solution we more frequently use.

In closing I should again like to compliment Dr Melick and his associates for the thorough manner in which they have investigated the use of these solutions and have proven the safety of the use of nonnecrotizing contrast solutions in renal arteriography. While these solutions are not as yet ideal so far as their contrast qualifications are concerned, nevertheless we are able to produce arteriograms that are sufficiently satisfactory and with a degree of safety that warrants the addition of this extremely valuable diagnostic procedure to the armamentarium of every urologist.

GEOGRAPHICAL DISTRIBUTION OF UROLOGISTS IN THE UNITED STATES

FRANKLIN FARMAN, LESLIE KAMENS AND RUTH G. McCANDLESS, A.B.

From the Robert S. Fox Urological Foundation, Whittier, Calif.

The original impetus for this study stems from the senior author's paper, published in 1931, surveying the distribution of urologists in the United States. Urology with its rapidly improving techniques was at that time a comparative newcomer in the ranks of the recognized surgical specialties, although actually it was well established and the American Urological Association itself had been founded in 1902. It was not surprising to note that the ratio of urological specialists (including nonmembers of the AUA) to population was very low—1.09 per 100,000 population, and that most of these specialists were located in, or very near, the larger cities. Now, after an interval of 20 years, we believe that a more complete and detailed analysis of the field of urological practice may delineate some significant comparisons, and perhaps forecast some future trends in this branch of the medical profession.

Primarily, we wished to determine how many urologists are now practicing, where they are located, and how this distribution of specialists relates to the growth and movement of the population of the country during the two decades under study. Of interest also are comparative figures of the distribution of physicians in general, and of the changing economic status of the various regional divisions of the United States.

The Bureau of the Census supplied us with the latest releases from the 1950 census, enabling us to make comparative density maps of the population of the United States for 1930 and 1950. These maps show graphically the great increase in population during this period, from 122 million to 150 million, an increase of nearly 23 per cent. The population growth may be attributed in large part to increase in the birth rate, lengthening of the span of life, and, to a lesser degree, to immigration. The medical profession can take due credit for the part it has played in this growth, although improved economic status, better housing, greater food consumption, and other social gains cannot be overlooked.

Clearly delineated in our county density maps, are the regional movements of the people, the three Pacific coast states showing a spectacular population gain, while the south, especially the Gulf states, is second in respect to both amount and rate of population increase. The effect of World War II was a major factor in this movement, with war workers migrating to the coastal industrial centers, and later, countless former service men settling in these attractive areas. Although the overall picture is one of population growth, many areas show a relative or even an actual decrease, particularly in the agricultural regions of the middle west. Here no doubt the modern technological developments in agriculture have been responsible for the release of many farm workers, who have relocated in urban and industrial areas.

The preparation of a map showing the location of urologists (members of

Read at annual meeting, Western Section American Urological Association, Sun Valley, Idaho, June 26, 1951.

GONADOTROPHIN TITER IN THE ADULT FEMALE THE EFFECT OF EJACULATION

WILLIAM H. MASTERS, DOROTHY T. MAGALON and MARY H. GORDY

From the Department of Obstetrics and Gynecology, Washington University School of Medicine,
St. Louis, Mo.

In the human female, cyclic variations in urinary gonadotrophins have been detected, especially in relation to ovulation, and physiological significance has been attributed to these variations. Fluctuations in male gonadotrophin titer, on the other hand, have been regarded as physiologically insignificant. A correlation was noted in this laboratory between the time of ejaculation and the subsequent increase in male urinary gonadotrophin titer. Such an increase might have a logical explanation, since it is well known that the stimulus of mating in the rabbit causes an abrupt increase in the excretion of gonadotrophin and that this, in turn, produces ovulation. In the male it might be supposed that the act of ejaculation could similarly cause a release of gonadotrophin so that the testis might be stimulated and spermatogenesis encouraged.

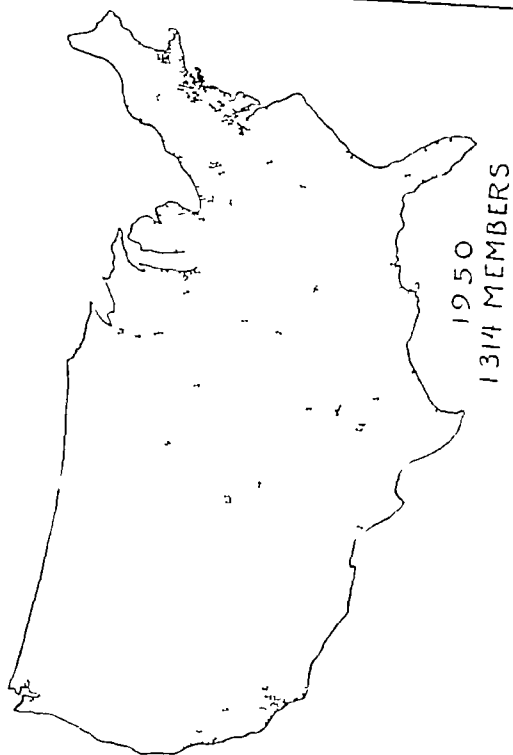
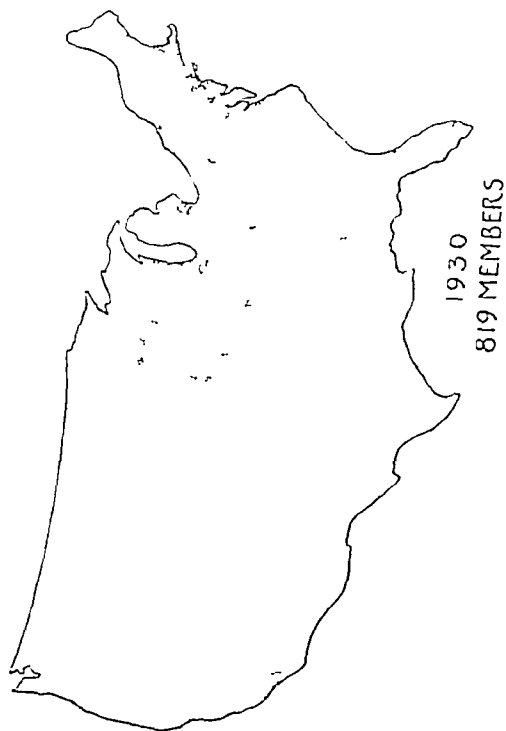
METHODS

Six physicians, four married and two single, ranging in age from 26 to 35 years, were used for the study. Daily 24 hour urine samples were collected by each individual for several consecutive days. Each new 24 hour collection period began at 6 00 p m. The specimens were refrigerated at approximately 40°F. In four specimens were secured for 28 day periods. In another case there were two collection periods, one of 17 days, and later, one of 9 days. A sixth subject collected over 28 days. A calendar was kept by each subject during the collection period denoting the days on which ejaculation occurred. Ejaculation generally occurred in the middle or late evening, within the first 6 hours after the start of the new 24 hour collection period. In another study of the same subjects, 6 hour fractional urine specimens were collected for 72 consecutive hours (a total of 12 specimens). Ejaculation had not occurred for at least 48 hours prior to the onset of the fractional collections. Ejaculation then took place in each case within the first 30 hours of collection. In four of the cases it was scheduled exactly at 24 hours, i.e., between the fourth and fifth fractional specimens.

Separation of the gonadotrophin from the urine was accomplished by the method of ultrafiltration through a nitrocellulose membrane, as described by Gorbman¹ in 1945. The hormone-containing residue was in every case kept in a calcium chloride desiccator for at least 24 hours before extraction. The dried residue of each specimen was then extracted with normal saline. Immature female mice aged 20-22 days and weighing from 6-8 gm were employed for bioassay. Aliquot portions of the extracts were administered intraperitoneally into each mouse at 24 hour intervals for three days. Twenty-four hours after the last injection, the mice were killed and individual uterine weights were measured.

¹ Gorbman, A. Ultrafiltration of urine for collection and biological assay of certain hypophyseal hormones. *J. endocrinol.* 37: 177-190, 1945.

GEOGRAPHICAL DISTRIBUTION OF UROLOGISTS IN THE UNITED STATES



Each dot represents one member of AUA

Tables 2 and 3 show a further breakdown of the complications. Surgical complications refer to those complications resulting directly from the operative procedure whereas the nonsurgical group refers to complications indirectly resulting from the operative procedure. The total number of deaths in each group and the cause of death are shown.

The great reduction in genito-urinary infection since 1934-37, 28.7 per cent to 7 per cent in 1946-49 and 6 per cent for the primary closure, can be seen.

TABLE 2. *Surgical complications*

	1934-37 SERIES		1946-49 SERIES (TELLMAN)		PRIMARY CLOSURE
	Trans- vesical	TUR	Trans- vesical	TUR	
Cardiovascular collapse					
Shock	13	2.0*	0	1.1	0
Hæmorrhage	0	0	0	1.1	1.0*
Rupture of bladder	—	1.0	—	1.1*	—
Total	13 ₁	3.0	0	3.3 ₁	1.0 ₁
Infection					
Septicæmia	13*	2.0**	0	0	1.0
Urinary sepsis	22.0	16.0	3.0	12.3	3.0
Cystitis	2.7	3.0	4.0	3.3	1.0
Wound sepsis	2.7	—	0	—	1.0
Total	28.7 ₁	21.0	7.0	15.6	6.0
Hæmorrhage without shock					
Immediate	6.8	1.0	3.0	3.3	4.0
Delayed	4.1	5.0	3.0	1.5	6.0
Total	10.9	6.0	6.0	7.8	10.0
Urinary	0	0	0.4*	0	0
Urinary sepsis permanent	—	—	0.4	—	1
Hæmaturia recurrent	—	—	—	0.6*	—
Prostatic abscess	—	0	—	1.1	—
Total	0	0	0	0	2

* One group of death of one mortality case.

** One group of death.

proph (no device gauge pack, Plicher type) in the retrophic approach and in the punic approach. Blood loss was slightly less than in the transurethral approach.

The use of whole blood during the operative or immediate postoperative periods has not only reduced the incidence of shock, but also aided greatly in the recovery from shock. (One of the 2 deaths in the primary closure series happened

TABLE 3. *Unsurgecal complications*

1914-19 SERIES	TRANSURETHRAL		PRIMARY CLOSURE	
	TVR	TRANSURETHRAL	TVR	TRANSURETHRAL

Pulmonary

Infect

Thrombotic

Myocardial

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period in an 80-year-old man who went into shock from excessive hemorrhage during the operation but from which he never recovered in spite of transfusions and other supportive therapy, succumbing 14 hours later.

Death by uremia is so infrequent today as to be negligible. Thomson-Walker in 1936 quoted 2.19 percent of the postoperative deaths following prostatectomy from uremia.

A lack of adequate follow-up permitted the incidence of incontinence to be given in only the 1914-19 transurethral and primary closure series. (One case in which group is listed.

The great reduction of complications of the non-surgical type in the primary closure series is outstanding. This is an indirect index of the less traumatic nature of the procedure compared to the pack or various large methods of hemo-

TABLE 4. *Wound complications in primary closure, transurethral prostatectomy*

Cause of death or mortality case	1914-19 SERIES		PRIMARY CLOSURE	
	TVR	TRANSURETHRAL	TVR	TRANSURETHRAL

Others

Thrombophlebitis-Phlebotrombosis

Fatal

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AUA) throughout the United States and Canada, was the next step in our survey. A single dot representing each urologist gives a density map for these specialists. Figure 1 shows a very much simplified sketch of this map, together with a similar diagram of urologist locations in 1930. These drawings illustrate graphically the great increase in membership of this group of specialists and the changes in their location throughout the country. The distribution of urologists as depicted on the maps roughly parallels that of the population in general, with greatest concentration in the heavily populated urban centers, and particularly heavy density in the eastern and Pacific coast areas.

The total number of urologists in the United States (listed in the AMA Medical Directory as "limited to the specialty") is 2,274. Of this number only 1,267, or 55.7 per cent, are members of the American Urological Association. (Total membership of AUA is 1,314, with 37 members in Canada, 5 in Cuba, 2 in

TABLE 1 *Examples of rank of states*

Population per square mile, per capita income, physicians per 100,000 population, urologists per 100,000 population

	1930				1950			
	Pop.	Inc.	Phys.	Urol.	Pop.	Inc.	Phys.	Urol.
Rhode Island	1	8	17	27	1	15	15	36
New York	5	1	3	5	5	1	1	3
Illinois	9	4	6	11	10	5	8	17
Louisiana	23	33	33	12	22	37	27	14
California	28	3	2	1	19	4	5	1
Florida	32	32	21	6	27	33	24	6
Nebraska	37	27	13	30	37	20	20	35
Idaho	43	31	43	46	43	25	41	47
Nevada	48	9	8	17	48	2	16	19

For complete tables of state ranks see appendix

Hawaii, 2 in the Canal Zone, and 1 in Puerto Rico.) The variation in percentage of AUA membership throughout the states ranges from 100 per cent in Rhode Island, Nevada, Idaho, Utah and Wyoming, to 0 per cent among 5 practicing urologists in New Mexico. No ready explanation for this phenomenon presents itself. Perhaps a preponderance of younger men, not yet qualified for membership, might be found in the larger metropolitan centers, but then how explain the 92.8 per cent membership in Maryland and 90.8 per cent in Massachusetts, while Illinois has 60 per cent, California 53 per cent, and Delaware only 14.3 per cent? This subject might merit further study. (For complete tabulation of percentage membership see appendix.)

Continuing our analysis we have made a study of state ranks according to 1) population per square mile, 2) per capita income, 3) physicians per 100,000 population, 4) urologists per 100,000 population (table 1). With the state of highest density designated as rank 1, the states are arranged in descending order of rank, and to facilitate comparisons, divided into four groups of twelve

PANEL DISCUSSION ON CARCINOMA OF BLADDER

Moderator, Charles C Higgins, Cleveland, O
 Collaborators, Hugh J Jewett, Baltimore, Md, William A Milner, Albany, N Y, Fathol-
 lah K Mostofi, Washington, D C, Vincent J O'Connor, Chicago, Ill

PRESENTATION OF SEVENTH ANNUAL AWARD FOR RESEARCH ON MALE REPRODUCTIVE
 TRACT By Reed M Nesbit, Chairman, Award Committee

RECIPIENT FOR 1952 Warren O Nelson, Ph.D, Professor of Anatomy, State University
 of Iowa College of Medicine, Iowa City, Iowa
 Address by Dr Nelson PROBLEMS OF TESTICULAR FUNCTION

STUDY OF THE HUMAN PROSTATE BY MEANS OF HISTOCHEMICAL INVESTIGATION (Second prize,
 essay contest)

Robert A. Kelley (by invitation), Charlottesville, Va

DISCUSSION WILLIAM P HERBST, Washington, D C
 WHAT SHOULD BE EXPECTED OF PROSTATIC SURGERY TODAY

David M Davis, Philadelphia, Pa

DISCUSSION SAMUEL A MacDONALD, Montreal, Quebec
 GRANULOMATOUS PROSTATITIS A CONDITION WHICH CLINICALLY MAY BE CONFUSED WITH
 CARCINOMA OF THE PROSTATE

Gershom J Thompson and (by invitation) Donald D Albers, Rochester, Minn

DISCUSSION LLOYD STOCKWELL, Kansas City, Mo
 CARCINOMA OF THE PROSTATE RESULTS OF TOTAL PROSTATECTOMY

Fletcher H Colby, Boston, Mass

DISCUSSION THOMAS E GIBSON, San Francisco, Calif

BLADDER TUMOR RECURRENCE IN THE URETHRA A WARNING

Joseph H Kiefer, Chicago, Ill

DISCUSSION HARRY M SPENCE, Dallas, Texas

SCIENTIFIC EXHIBIT*

Dr Samuel A Vest, Chairman

1 Physiology of the Uretero-intestinal Anastomosis

Roger Baker (by invitation), Chicago, Ill

2 Plastic Procedures on the Urinary Bladder

Roger W Barnes and (by invitation) William M Wilson, Henry L Hadley, Stanley
 E Farley and R Theodore Berman, Los Angeles, Calif

3 Paraplegia Resulting from Carcinoma of the Prostate

Henry I Berman and (by invitation) G L Suder, Dayton, O

4 Femoro iliac Phlebography by Injection of the Dorsal and Lateral Veins of the Penis

William H Boyce and John H deTar (by invitation), Charlottesville, Va

5 The "Squat Shot" or Dorsal Cystogram A Technique for Roentgenography of the Posterior
 Bladder and Pelvic Ureters

William H Boyce and James A Harris (by invitation), Charlottesville, Va

6 Delayed Cystograms

Raymond G Bunge, Iowa City, Iowa, and Charles M Stewart, Los Angeles, Calif

7 Treatment and Prevention of Kidney Stone by Increasing Protective Urinary Colloids with
 Hyaluronidase

Arthur J Butt, Pensacola, Fla, and (by invitation) Ernst A Hauser, Cambridge,
 Mass, and Joseph Seifter, Philadelphia, Pa

8 Prostatic Perineal Punch Biopsy

George F Cahill and (by invitation) Ralph J Veenema, New York, N Y

9 Photographic History of the American Urological Association

Wirt B Dakin, Los Angeles, Calif

10 Effect of Banthine on the Urinary Tract

John W Draper and (by invitation) Stewart Wolf, Howard Kravetz and John F Mur-
 phy, New York, N Y

11 Transcervical Repair of Complicated Vesicovaginal Fistula

Franklin Farman and (by invitation) Leshe Kamens and James Hollowtier,
 Calif

12 Giant Hydronephrosis

Reginald A Hancock, Pittsburgh, Pa

13 A New Resectoscope and Ureteral Catheter Connector

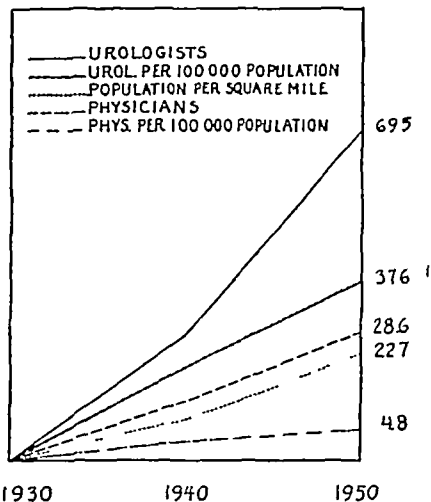
S P R Hutchins and J Reese Blundell (by invitation), Houston, Texas

* The Scientific Exhibit has been erected under the supervision of the Director of Ex-
 hibits, Mr William P Didusch

states each, defined as high, middle high, middle low and low. From the tables of state ranks (see appendix) we present a few salient features, with a brief tabulation of results in representative states from various parts of the country. The District of Columbia, which stood first in all categories, has been disregarded in the determination of ranks, since it is almost entirely urban, and not strictly comparable to the 48 true states.

In the population ranks it is interesting to note that Rhode Island still holds first place, its population density having increased from 644.3 persons per square mile in 1930 to 724.1 in 1950. Nevada still ranks last, although its population has nearly doubled (from 0.8 to 1.4 per square mile). California has moved

POPULATION, PHYSICIAN AND UROLOGIST INCREASES



Population of the United States

1930	122,755,046	
1940	131,669,275	7.2% Increase
1950	150,697,361	22.7% Increase

Physicians in the United States

1930	156,406	
1940	175,382	12.0% Increase
1950	201,277	28.6% Increase

Physicians per 100,000 Population

1930	127.4	
1940	133.2	4.5% Increase
1950	133.5	4.8% Increase

Urologists in the United States

1930	1,341	
1940	1,734	29.3% Increase
1950	2,274	69.5% Increase

Urologists per 100,000 Population

1930	1.09	
1940	1.31	20.1% Increase
1950	1.50	37.6% Increase

up from twenty-eighth to nineteenth place (37.5 to 67.4 per square mile), New York, while increasing from 264.2 to 309.3 still holds fifth place in the ranks. In Nebraska the population has remained practically stationary at 17.9 per square mile, with thirty-seventh rank in both cases.

Further study of the tabulations reveals numerous facets for discussion or speculation. In per capita income New York continues to hold first rank, while Nevada has moved up from ninth to second place. New York has risen from third to first place in physician concentration, and from fifth to third in urologists, Nevada on the other hand, has dropped from eighth to sixteenth in physicians, and from seventeenth to nineteenth in urologists. The southern states (all but Florida in the lowest income group) show surprisingly high concentrations of medical men, and particularly urological specialists. California main-

- 14 *Transurethral Prostatectomy Modification of Resectoscope*
José Iglesias de la Torre (by invitation), Havana, Cuba
- 15 *Signposts of Urological Disease in Infants and Children*
S Harris Johnson, III and (by invitation) Bertram R Girdany, Pittsburgh, Pa
- 16 *Peristalsis of the Upper Urinary Tract*
Thomas H Johnson (by invitation), New York, N Y
- 17 *Specific Antibacterial Therapy in Urology*
R Frank Jones (by invitation), Washington, D C
- 18 *A Histochemical Study of the Human Prostate*
Robert A Kelley and J F A McManus (by invitation), Charlottesville, Va
- 19 *Subcapsular Nephrectomy*
Col James C Kimbrough and (by invitation) Capt W H Morse, Washington, D C
- 20 *Effect of Banthine on the Normal and Neurogenic Bladder*
Jack Lapides and Austin I Dodson, Jr (by invitation), Ann Arbor, Mich
- 21 *A New Recording Cystometer*
Paul R Leberman and (by invitation) John J Murphy and D Franklin Milam, Philadelphia, Pa
- 22 *Vesical Mucosal Grafts Experimental Studies and Application in Hypospadias*
Victor F Marshall and (by invitation) Robert Spellman, New York, N Y
- 23 *A New Concept of Bladder Innervation and its Relationship to Abdomino perineal Proctosigmoidectomy*
Lowrain E McCrea, Philadelphia, Pa
- 24 *The Role of the Urine in Vesical Carcinoma*
Donald F McDonald (by invitation), Seattle, Wash
- 25 *Excretory Urography in the Diagnosis of Ureteropelvic Obstruction*
William L McLaughlin (by invitation), John P Bowler and (by invitation) William C MacCarty, Jr, Hanover, N H
- 26 *Atlas of Tumor Pathology, Male Sex Organs*
Mary Ruth Oldt, Frank J Dixon and Robert A Moore (by invitation), Washington, D C
- 27 *Pneumography as Applied to Urology*
J Sydney Ritter and (by invitation) William Shehadi and Alfred Johnson, New York, N Y
- 28 *Physiology of Hyperchloremia after Ureterosigmoidostomy*
Milton L Rosenberg (by invitation), San Francisco, Calif
- 29 *Uretero-arachnoid Anastomosis in the Treatment of Hydrocephalus*
Edgar A Slotkin, Buffalo, N Y
- 30 *A Nonopaque Radiographic and Water Repellent Examining Table Mat*
Moses Swick, New York, N Y
- 31 *Skin Ureterostomy through a Pedicle Flap*
Herbert S Talbot, Framingham, Mass
- 32 *The Microscopic Circulation of the Tuberculous Kidney*
Wallace S Tirman and Truman E Caylor (by invitation), Bluffton, Ind
- 33 *Demonstration of Renal Arterial Pattern in Man and Animal, both Normal and Pathologic*
Parke G Smith, Miami, Fla
- 34 *Hypobaric Pontocaine Spinal Anesthesia for Urological Operations in Lateral Position*
William F Brehm and William Baurys, Sayre, Pa

TECHNICAL EXHIBIT

MR WILLIAM P DIDUSCH, *Director*

NAME AND ADDRESS OF FIRM	BOOTH NO
ABBOTT LABORATORIES, North Chicago, Ill	33
ADELPHI SURGICAL Co, Inc, Brooklyn, N Y	23
AMERICAN CYSTOSCOPE MAKERS, INC, New York, N Y	3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15
C R BARD, Inc, New York, N Y	41, 42, 43, 44
BIRTCHE CORPORATION, Los Angeles, Calif	16
CIBA PHARMACEUTICAL PRODUCTS, Inc, Summit, N J	25
CLINICAL SPECIALTIES, St Paul, Minn	46
COCA COLA COMPANY, Atlanta, Ga	20
EATON LABORATORIES, Norwich, N Y	25
GRUNE AND STRATTON, Inc, New York, N Y	34
HOMEMAKERS' PRODUCTS CORP, New York, N Y	47
LIEBEL-FLARSHEIM Co, Cincinnati, O	31, 32
J B LIPPINCOTT Co, Philadelphia, Pa	20
MALLINCKRODT CHEMICAL WORKS, St Louis, Missouri	22, 23
MERCK AND Co, Inc, New York, N Y	49
WILLIAM S MERRELL Co, Cincinnati, O	21

tains a high rank in both income and urologist concentration in both decades, but now shows a decrease in ratio of general physicians per unit of population

A digest of the total results of our survey is shown in figure 2

As the graph clearly shows, the curve of population rises gradually during the years 1930 to 1940, and at a much accelerated rate in the following decade. The physicians in the country increased at a rate somewhat greater than the population during the first ten years, but the rate of increase per unit of population leveled off during the second decade, so that the number of physicians per 100,000 people showed only the very small increase of 4.8 per cent for the entire period. The growth of urology during the twenty year period is strikingly shown in the graph, a 69.5 per cent numerical increase, and 37.6 per cent increase in ratio of urologists to unit population. Whereas in 1930 there were 1.09 urological specialists for every 100,000 people, today there are 1.50 (limited to the specialty) per unit of population.

Several factors relevant to the urological increment may be offered. The effects of World War II no doubt brought about profound changes in the thinking of numerous younger medical men. Such young doctors, their training interrupted by the conflict, on return to civilian life felt the need for professional advancement. Urology, a surgical specialty with highly developed techniques, offered a stimulating challenge to these younger physicians. Much credit for the urologist increase is also undoubtedly due to improved teaching, on both undergraduate and resident levels. The pioneer work of the older practicing urologists, their scientific endeavors and publications, have also led many younger doctors into the field of urology.

A statistical survey such as we have just completed, the primary purpose of which is to portray an accurate picture of conditions as they now exist, hardly seems to justify any "conclusions." However, it seems pertinent to note that the great increase in urological specialists herein demonstrated indicates an improvement in service rendered by the medical profession to the American people, making more careful diagnosis and skillful care available to greater numbers of persons. A decentralization of urologists would seem a desirable development for the welfare of the public and the profession itself. Whether such a movement away from densely populated urban centers is likely to occur in the period ahead, depends on so many political, economic and military factors, that it would be a bold prophet indeed who would hazard a prediction.

304 V Painter Ave, Whittier, Calif

V MUELLER & COMPANY, Chicago, Ill	37, 38
NEPERA CHEMICAL Co Inc, Yorkers, N Y	24
OHIO CHEMICAL AND SURGICAL EQUIPMENT Co, Madison, Wis	25
PARKE, DAVIS AND COMPANY, Detroit, Mich	35
CHARLES PFIZER AND Co, Inc, Brooklyn, N Y	1
RADIUM CHEMICAL Co, Inc, New York, N Y	2
RADIUM EMANATION CORPORATION, New York, N Y	39
W B SAUNDERS Co, Philadelphia, Pa	27
SCHERING CORP, Bloomfield, N J	45
E R. SQUIBB AND SONS, New York, N Y	19
WILLIAMS AND WILKINS Co, Baltimore, Md	36
WINTHROP-STEARNs, Inc, New York, N Y	17, 18

APPENDIX

1950 TABLE OF STATE RANKS

POPULATION PER SQUARE MILE			PER CAPITA INCOME		PHYSICIANS PER 100,000 POPULATION		UROLOGISTS PER 100,000 POPULATION	
	D of C		D of C		D of C		D of C	
1	R I	12,865 6	N Y	\$1,820	N Y	309 1	Calif	4 64
2	N J	724 1	Nev	1,758	Mass	204 9	Del	2 25
3	Mass	641 8	Del	1,731	Colo	186 3	N Y	2 21
4	Conn	582 2	Calif	1,675	Conn	165 0	Conn	2 19
5	N Y	413 8	Ill	1,665	Calif	164 2	Colo	2 10
6	Md	309 3	Conn	1,618	Vt	158 8	Fla	2 06
7	Penna	233 8	N J	1,591	Md	151 8	Mass	1 79
8	Ohio	233 3	Wyo	1,546	Ill	148 2	Vt	1 63
9	Del	193 9	Wash	1,481	Minn	146 9	Mo	1 59
10	Ill	161 6	Ore	1,469	N H	138 9	Ga	1 53
11	Mich	154 9	Mich	1,448	Penna	138 7	Penna	1 42
12	Ind	109 7	Ohio	1,443	Del	135 8	Wash	1 41
		108 8		1,436		135 7		1 39
13	W Va	83 2	Mass	1,417	N J	133 3	Ore	1 38
14	N C	82 9	Penna	1,416	Mo	129 0	La	1 36
15	Va	81 2	R I	1,403	R I	127 3	N H	1 32
16	Tenn	78 8	Md	1,401	Nev	125 9	Ind	1 32
17	Ky	72 7	Mont	1,390	Ohio	125 1	Ill	1 32
18	S C	69 1	Colo	1,386	Utah	122 6	N J	1 30
19	Calif	67 4	Wis	1,329	Kans	122 4	Nev	1 26
20	Wash	64 1	Nebr	1,294	Nebr	119 9	Tenn	1 24
21	Wis	61 9	Ia	1,292	Ore	119 2	Tex	1 21
22	La	58 7	Ind	1,290	Wash	114 8	Md	1 20
23	N H	58 6	Mo	1,286	Ia	110 6	Ohio	1 17
24	Ga	58 4	Minn	1,227	Fla	110 6	Okla	1 17
25	Mo	57 2	Ida	1,221	Mich	109 9	Mich	1 12
26	Ala	55 2	Utah	1,213	Ind	109 8	Wis	1 11
27	Fla	49 1	Kans	1,210	La	109 2	W Va	1 10
28	Ia	47 2	Tex	1,205	Wis	108 0	N C	1 09
29	Miss	46 9	N D	1,202	Ariz	107 6	Ia	1 03
30	Vt	41 2	N H	1,195	Me	106 9	S C	99
31	Minn	36 7	S D	1,174	Tex	100 6	Ala	93
32	Ark	36 2	Ariz	1,165	Okla	97 3	Me	93
33	Okla	32 0	Fla	1,102	Mont	95 2	Minn	94
34	Me	30 4	Me	1,087	Va	95 2	Ariz	93
35	Tex	28 2	Vt	1,075	Tenn	94 8	Nebr	91
36	Kans	23 1	Okla	1,068	Ga	88 3	R I	89
37	Nebr	17 9	Va	1,039	W Va	87 7	Mont	85
38	Ore	15 8	N Mex	1,033	Ark	87 6	Va	79
39	Colo	12 7	La	1,002	Wyo	85 7	Utah	74
40	N D	8 8	W Va	998	Ky	84 4	N Mex	74
41	S D	8 4	Ga	876	Ida	82 7	N D	66
42	Utah	8 3	Tenn	873	N C	81 1	Ark	57
43	Ida	7 0	Ky	865	N D	76 9	Ky	57
44	Ariz	6 5	N C	854	S D	75 5	Kans	53
45	N Mex	5 5	S C	787	N Mex	74 4	S D	46
46	Mont	4 1	Ark	778	Ala	71 8	Miss	41
47	Wyo	2 9	Ala	773	S C	70 0	Ida	34
48	Nev	1 4	Miss	634	Miss	67 0	Wyo	34

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POPULATION PER SQUARE MILE		PER CAPITA INCOME		PHYSICIANS PER 100 000 POPULATION		UROLOGISTS PER 100 000 POPULATION		
1	D of C	7,852 7	D of C	\$1,191	D of C	377 5	D of C	4 75
2	R. I	644 3	N Y	1,125	Colo	183 2	Calif	1 85
3	N J	537 8	N J	947	Calif	178 0	Wash	1 79
4	Mass	528 6	Calif	946	N Y	166 9	Del	1 67
5	Conn	333 4	Ill	932	Mo	155 4	Mo	1 65
6	N Y	264 2	Del	919	Mass	155 2	N Y	1 62
7	Penna	214 8	Conn	918	Ill	149 0	Fla	1 56
8	Md	164 1	Mass	897	Md	148 9	Md	1 54
9	Ohio	163 1	R I	851	Nev	143 8	Colo	1 54
10	Ill	136 2	Nev	817	Vt	138 7	Ore	1 46
11	Del	121 3	Penna	767	Conn	134 7	Mass	1 27
12	Ind	89 8	Ohio	748	Ore	133 6	Ill	1 26
13	Mich	84 2	Mich	745	Ohio	130 3	La	1 19
14	W Va	72 0	Wash	713	Nebr	129 4	Tex	1 17
15	Ky	65 1	Md	703	Penna	125 1	Okla	1 12
16	N C	65 0	Wyo	687	Me	124 1	Vt	1 11
17	Tenn	62 8	N H	652	Wash	122 8	Tenn	1 11
18	Va	60 2	Ore	640	R I	122 7	Nev	1 09
19	Wis	53 2	Wis	634	Ind	122 6	Ohio	1 05
20	Mo	52 8	Colo	616	Ia	122 4	Ind	1 05
21	Ala	51 6	Mo	612	N H	121 8	Ga	1 03
22	N H	51 5	Mont	602	Fla	120 1	Penna	99
23	Ga	49 5	Vt	601	Minn	119 9	S C	98
24	La	46 3	Ind	583	Del	116 6	Conn	93
25	S C	45 0	Ariz	573	Mich	115 8	Ariz	92
26	Ia	44 5	Minn	566	Kans	115 2	N C	91
27	Miss	43 4	Me	566	Tenn	113 2	Me	88
28	Vt	39 4	Nebr	557	Tex	111 1	R I	87
29	Calif	36 5	Ia	546	Ariz	111 1	Mich	87
30	Ark	35 3	Utah	537	Ky	109 6	Utah	79
31	Okla	34 5	Kans	532	N J	107 8	Nebr	79
32	Minn	31 7	Ida	518	Ark	106 6	Va	78
33	Fla	26 8	Fla	484	Va	106 6	W Va	75
34	Me	26 7	Tex	465	Wis	105 6	N Mex	70
35	Wash	23 4	W Va	464	Wyo	104 2	Wis	68
36	Kans	23 0	Okla	455	Okla	103 7	N J	61
37	Tex	22 2	Va	422	W Va	103 0	Ky	61
38	Nebr	17 9	S D	417	Ga	99 2	Ala	60
39	Ore	10 0	La	415	La	98 7	Ia	56
40	Colo	10 0	N D	387	Utah	96 3	Ark	54
41	N D	9 7	Ky	371	Mont	90 2	Kans	53
42	S D	9 0	Tenn	349	N Mex	87 8	Wyo	44
43	Utah	6 2	N Mex	338	S D	84 4	Minn	42
44	Ida	5 3	Ga	329	Ida	84 0	N H	41
45	Ariz	3 8	N C	309	Ala	80 3	Mont	37
46	Mont	3 7	Ala	305	Miss	77 9	Miss	29
47	N Mex	3 5	Ark	305	N D	75 6	Ida	22
48	Wyo	2 3	Miss	273	N C	74 8	N D	14
49	Nev	8	S C	252	S C	74 3	S D	14

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STATE	UROLOGISTS*	AUA MEMBERS	% MEMBERSHIP
Alabama	30	12	40%
Arizona	7	3	42 8%
Arkansas	11	5	45 4%
California	229	122	53 1%
Colorado	27	16	59 0%
Connecticut	42	21	50 0%
Delaware	7	1	14 3%
District of Columbia	37	26	70 0%
Florida	48	34	70 0%
Georgia	48	19	39 5%
Idaho	2	2	100 0%
Illinois	115	70	60 0%
Indiana	52	35	67 3%
Iowa	27	18	66 6%
Kansas	10	6	60 0%
Kentucky	17	11	64 7%
Louisiana	36	23	63 9%
Maine	9	7	77 7%
Maryland	28	26	92 8%
Massachusetts	76	69	90 8%
Michigan	71	45	63 4%
Minnesota	28	23	82 1%
Mississippi	9	3	33 3%
Missouri	60	44	73 3%
Montana	5	1	20 0%
Nebraska	12	11	91 7%
Nevada	2	2	100 0%
New Hampshire	7	5	71 4%
New Jersey	63	35	55 5%
New Mexico	5	0	0%
New York	324	213	65 7%
North Carolina	44	26	59 0%
North Dakota	4	1	25 0%
Ohio	93	57	61 3%
Oklahoma	26	9	34 6%
Oregon	21	9	42 8%
Pennsylvania	148	99	66 9%
Rhode Island	7	7	100 0%
South Carolina	21	12	57 1%
South Dakota	3	2	66 6%
Tennessee	41	27	65 9%
Texas	93	44	47 3%
Utah	5	5	100 0%
Vermont	6	3	50 0%
Virginia	26	15	57 7%
Washington	33	19	57 6%
West Virginia	22	16	72 8%
Wisconsin	38	18	47 4%
Wyoming	1	1	100 0%

* Listed in AMA Medical Directory as "limited to the specialty"

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October 8-11, 1952

Northeastern Section

Cruise to Bermuda, aboard the
S S Ocean Monarch
October 4-10, 1952

Southeastern Section

Hotel de Nacional, Havana, Cuba
March 26-29, 1953

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Any candidate who starts training before June 30, 1955, under the old requirements, may complete the program of the old requirements and thereby become acceptable for examination. No more candidates will be accepted for examination whose training has been entirely on a preceptorship basis started after March 1, 1951.

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ASSOCIATION, CHALFONTE-HADDON HALL, ATLANTIC
CITY, N J, JUNE 23, 24, 25, 26, 1952

JUNE 23

Motion Pictures

PENECTOMY FOR CARCINOMA

Leander W Riba, Chicago, Ill

THE TECHNIQUE OF TRANSLUMBAR AND PERCUTANEOUS FEMORAL ARTERY CATHETERIZATION AORTOGRAPHY COMBINED WITH RETROPERITONEAL OXYGEN INJECTION

Willard E Goodwin and Robert C Walter (by invitation) and Gilbert J Thomas, Los Angeles, Calif

TRANSLUMBAR RENAL ARTERIOGRAPHY

Col James C Kimbrough and (by invitation) Capt William H Morse, Washington, D C

Scientific Sessions

PYELOGRAPHY IN COMBINATION WITH SIMULTANEOUS RETROPERITONEAL PNEUMOGRAPHY

John Duff, Herbert R Kenyon and (by invitation) Richard M Hyman, New York, N Y

PERIRENAL AIR INSUFFLATION BY THE PARACOCYGEAL ROUTE

Samuel H Rothfeld (by invitation) and Frank C Hamm, Brooklyn, N Y

DISCUSSION GEORGE F CAHILL, New York, GILBERT J THOMAS, Santa Monica, Calif

THE UROLOGICAL IMPORTANCE OF RADIOPAQUE APPENDICEAL CONCRETIONS

George C Prather and (by invitation) James A Singiser, Brookline, Mass

DISCUSSION ROBERT LICH, JR, Louisville, Ky

ADRENALECTOMY

Richard W Satterthwaite, Ancon, Canal Zone

DISCUSSION J HARTWELL HARRISON, Boston, Mass

EFFECT OF INCREASING PROTECTIVE URINARY COLLOIDS WITH HYALURONIDASE IN THE TREATMENT AND PREVENTION OF RENAL CALCULI

Arthur J Butt, Pensacola, Fla and (by invitation) Ernst A Hauser, Cambridge, Mass, Joseph Seifter, Philadelphia, Pa and Joseph Q Perry, Pensacola, Fla

DISCUSSION LINWOOD D KEYSER, Roanoke, Va, BENJAMIN S ABESHOUSE, Baltimore, Md

SUBCAPSULAR NEPHRECTOMY

Col James C Kimbrough and (by invitation) Capt W H Morse, Washington, D C

DISCUSSION DANIEL R HIGBEE, Denver, Colo

JUNE 24

Motion Pictures

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John K Lattimer, New York, New York

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ACCIDENTAL INJURIES TO URINARY STRUCTURES

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DISCUSSION SAMUEL A VEST, Charlottesville, Va

GENITO-URINARY TRACT INJURIES IN COMBAT

Col Joseph P Russell and Capt Charles Henkel (by invitation), Tokyo Army Hospital, Far East Command

DISCUSSION JOHN F PATTON, St Louis, Mo

LATE RENAL COMPLICATIONS OF PARAPLEGIA, III TREATMENT OF VESICO URETERAL REFLUX BY SKIN URETEROSTOMY THROUGH A PEDICLE FLAP

Herbert S Talbot and (by invitation) David P Paull and George R Read, Framingham, Mass

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THE USE OF RHIZOTOMY IN THE TREATMENT OF THE ADVANCED PARAPLEGIC BLADDER
Herbert Brendler, Erich Krueger and Philip Lerman (by invitation) and Archie L Dean, New York, N Y

DISCUSSION GEORGE W FISH, New York, N Y, R CARL BUNTS, Richmond, Va

HOMOLOGOUS TRANSPLANTATION OF HUMAN KIDNEYS

David M Hume, John P Merrill, Benjamin F Miller and George W Thorn (by invitation), Boston, Mass

DISCUSSION CARL DAVIS, JR (by invitation), Chicago, Ill, JOHAN N DEKLERK (by invitation), Baltimore, Md, GEORGE HAAS (by invitation), Chicago, Ill

NEW DEVELOPMENTS IN THE CHEMOTHERAPY OF RENAL TUBERCULOSIS
John K Lattimer and Archie L Dean, New York, N Y

DISCUSSION FREDERICK A LLOYD, Chicago, Ill

THE TYPE AND DISTRIBUTION OF CHOLINE ESTERASES OF THE URINARY COLLECTING SYSTEM OF THE DOG THEIR RELATIONSHIP TO URETERAL PERISTALSIS AND POSSIBLE ROLE IN CONGENITAL ANOMALIES (*Third prize, essay contest*)
Johan DeKlerk (by invitation) Baltimore, Md

DISCUSSION JACK LAPIDES (by invitation), Ann Arbor, Mich

JUNE 24

Motion Pictures

ANATOMICAL DISSECTION OF THE FEMALE PERINEUM

R Theodore Bergman, Los Angeles, Calif

FEMALE URETHRAL DIVER TICULECTOMY

Charles M Stewart, Los Angeles, Calif

REPAIR OF VESICOVAGINAL FISTULA

Oswald S Lowsley, New York, N Y

A SIMPLIFIED PROSTATIC BIOPSY PUNCH

Ralph J Veenema (by invitation) and George F Cahill, New York, N Y

RADICAL RETROPUBIC PROSTATECTOMY FOR CANCER

John K Lattimer, New York, N Y

ONE-STAGE TOTAL CYSTECTOMY FOR INFILTRATING TUMORS OF THE BLADDER AND PROSTATE

Jose Iglesias de la Torre (by invitation), Havana, Cuba

URETEROSIGMOIDOSTOMY SIMPLIFIED TECHNIQUE

W Calhoun Stirling and (by invitation) C H Ligon, Washington, D C

RETROPUBIC PROSTATECTOMY

Robert Lich, Jr and (by invitation) Joseph E Maurer, Louisville, Ky

INTUBATED URETEROTOMY

David M Davis, Philadelphia, Pa

A TECHNIQUE FOR REPLACING A URETERAL SPLINT PREMATURELY OR ACCIDENTALLY REMOVED

J Robert Rinker, Augusta, Ga

JUNE 25

Motion Pictures

ANATOMICAL DISSECTION OF THE POSTERIOR LUMBAR REGION

R Theodore Bergman, Los Angeles, Calif

CALYCECTOMY

Oswald S Lowsley, New York, N Y

SUBCAPSULAR NEPHRECTOMY

Col James C Kimbrough and (by invitation) Maj Evan L Lewis, Washington, D C

Scientific Sessions

DELATED CYSTOGRAMS

Charles M Stewart, Los Angeles, Calif

DISCUSSION GEORGE H EWELL, Madison, Wis

THE PHYSIOLOGY OF HYPERCHLOREMIC ACIDOSIS FOLLOWING URETEROSIGMOIDOSTOMY
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DISCUSSION OSWALD S LOWSLEY, New York, N Y

THE EFFECT OF BANTHINE IN THE TREATMENT OF GENITO-URINARY DISORDERS
John W Draper and (by invitation) Stewart Wolf, Howard Kravetz and John F Murphy, New York, N Y

DISCUSSION REED M NESBIT, Ann Arbor, Mich

THE DIVERSION OF URINE BY URETEROSTOMY-IN-SITU
Samuel N Vose and (by invitation) Grant M Dixey, Boston, Mass

DISCUSSION FRANCIS P TWINEM, New York, N Y

CURRENT STATUS OF UROLOGY IN THE ARMY

May Gen George E Armstrong, Surgeon General United States Army, Washington, D C

HISTOPATHOLOGICAL STUDY OF RENAL TUBULAR REACTION FOLLOWING INTRAVENOUS INFUSION OF HOMOLOGOUS HEMOGLOBIN SOLUTION IN DOGS (*Honorable mention, essay contest*)

Alex L Finkle (by invitation), New York, N Y

DISCUSSION C D CREEVY, Minneapolis, Minn

THE CLINICAL EFFECT OF PITUITARY ADRENOCORTICOTROPHIC HORMONE ON CHRONIC INTERSTITIAL CYSTITIS

Albert J Paquin (by invitation) and Victor F Marshall, New York, N Y

THE USE OF CORTISONE IN INTERSTITIAL CYSTITIS

John E Dees, Durham, N C

DISCUSSION PAUL R LEBERMAN, Philadelphia, Pa, THOMAS L SCHULTE,
San Francisco, Calif

JUNE 25, 1952

PRESIDENTIAL ADDRESS WHAT OF THE FUTURE?

DR ELMER HESS, Erie, Pa

THE RAMON GUITERAS LECTURE ENDOCRINE FACTORS IN CANCER

DR CHARLES HUGGINS, Professor of Urology and Director of the Ben May Laboratory for Cancer Research, University of Chicago, Chicago, Ill

JUNE 26

Motion Pictures

LEONARD-SKEGGS ARTIFICIAL KIDNEY

Walter A Keitzer, Akron, Ohio

NEPHRECTOMY RUPTURED KIDNEY

Austin H Wood, Baltimore, Md

SKIN URETEROSTOMY THROUGH A PEDICLE FLAP

Herbert S Talbot and (by invitation) David P Paull, Framingham, Mass

Scientific Sessions

CARCINOMA COMPLICATING VESICAL DIVERTICULUM

Raymond F Mayer and Thomas D Moore, Memphis, Tenn

DISCUSSION HAROLD A O'BRIEN, Dallas, Texas

BLADDER NEOPLASMS A REVIEW OF OVER 2500 BIOPSIES AND SPECIMENS

Meyer M Melicow, New York, N Y

DISCUSSION ALBERT E BOTHE, Philadelphia, Pa

PRIMARY CARCINOMA OF THE MALE URETHRA

William J Baker and (by invitation) Edwin C Graf and John Vandenberg, Chicago, Ill

DISCUSSION LOWRAIN E MCCREA, Philadelphia, Pa

PLASTICS PROCEDURES ON THE URINARY BLADDER

Roger W Barnes, R Theodore Bergman and (by invitation) William M Wilson, St. Louis, E Farley and Henry L Hadley, Los Angeles, Calif

DISCUSSION NELSE F OCKERBLAD, Kansas City, Mo

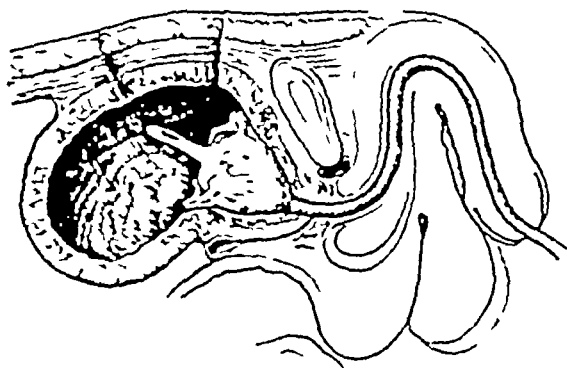
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state control in prostatectomy. The incidence of these complications in the 1934-37 transurethral prostatectomy series is very large—33 per cent—but this was reduced to 15.3 per cent in the 1946-49 series, and further reduced to 5 per cent in the primary closure series. This compares favorably and is slightly less than the 1946-49 transurethral resection group, 6.6 per cent. This latter procedure is noted for its minor traumatic assault on the heart and lungs.

TABLE 1. Comparison of various methods of hemostasis in transurethral prostatectomy (After Tellman)

	CYSTOTOMY TUFF WITH CAULZ PACK	CYSTOTOMY TUBE WITH FULTHER PAC	CYSTOTOMY TUBE WITH OXACEL AND CATHETER	PRIMARY CLOSURE WITH OXACEL AND CATHETER
Number of cases	36	75	33	23
Fatal days	6	4	3	3
Bed confinement	14 (II)*	8 (II)	6 (II)	6 (II)
Tolerated hospital diet	5th day	4th day	3rd day	2nd day
Discharge ambulation	10th day	7th day	4th day	2nd day
Cathome tube or catheter drainage	20 days	17 days	15 days	8 days
Complications	9	18	4	4
Postoperative hospitalization	25 days	22 days	15 days	13 days

* 1 hypodermic injection



A study of wound complications, table 4 is given only for the primary closure series as the hospital charts were too inadequate for an accurate analysis in the other series. In 17 per cent of the cases the patients developed some degree of suprapubic urinary leakage. By closing primarily this becomes a new complication. In itself it is not serious, except to prolong hospitalization. The use of chloromycetin routinely postoperatively, and the use of the transverse incision in the bladder seem to have lowered this incidence in the most recent cases. One case of wound infection and one case of wound hematoma are the only other wound complications listed.

Table 5 prepared by Tellman⁶ at the time we had performed 23 primary closures in which the various other methods of transvesical prostatectomy were analyzed and compared is reprinted.

Detail of the procedure is given in the original article. Some noteworthy changes have been made since then.

Aside from the routine transvesical approach in which we have stressed minimal dissection of the perivesical tissues, we now make a transverse cystotomy incision to prevent tearing the bladder toward the vesical neck during enucleation. This likewise simplifies closure of the bladder.

After enucleation of the prostate the fossa is packed for 5 minutes with a hot pack. A thin layer of oxidized cellulose in the form of a cone is wrapped around a distended Foley bag catheter and brought down snugly into the vesical neck, folding the edges outward (fig. 1). We recently have used, with much success, a 22½ modified Coppridge catheter with a 75 cc bag. The short whistle tip gives better drainage and irrigation. This type of bag permits filling from 30 cc to 75 cc so that it can be used to fit various sized prostatic fossae. The catheter is held under slight tension until the conclusion of the operation when it is taped firmly to the thigh.

The bladder is closed in two layers. We use a running suture for each layer and the second suture line catches the first so that a potential space for extravasation or infection between the bladder layers will not exist. Tension on the catheter is maintained from three to six hours. The space of Retzius is drained for three to five days.

The water is removed from the Foley bag the next morning and nearly all the oxidized cellulose can be washed free at this time. The modified Coppridge catheter is converted into a straight inlying catheter. The catheter, however, may be changed at any time. Usually it is removed on the sixth postoperative day and the patient permitted to void.

CONCLUSION

One stage transvesical prostatectomy with primary closure using oxidized cellulose and a Foley catheter for hemostasis when compared with other methods of transvesical prostatectomy employing some form of vesical pack, bag, or drain results in a lower total hospitalization, a decrease in postoperative hospital days, a low incidence of urinary sepsis, and a marked decrease in surgical complications particularly of the indirect nature. Mortality was 2 per cent.

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a tooth extraction. This fact prompted a complete study of the blood. An elevated blood alkaline phosphatase was the single abnormal finding. The diagnosis of Paget's disease was confirmed by x-ray examination. See table 1. There was no residual urine. Penicillin, 300,000 u, streptomycin gm 1 and vitamin C 100 mg were given daily. Morphine sulfate $\frac{1}{2}$ gr and scopolamine $\frac{1}{200}$ gr were given as pre-anesthetic medication. Pentothal sodium, nitrous oxide anesthesia was used. It was supplemented with ether. The prostate gland weighed 101 gm. Morphine sulfate $\frac{1}{2}$ gr was given every 4 hours for postoperative pain. Moderate bleeding was noted when the patient was returned to bed. The bleeding persisted and became so profuse and uncontrollable that the patient was returned to the operating room 12 hours after the prostatectomy. Three transfusions of 500 cc whole blood was given during this interval. The surgical incision was opened and the bleeding controlled with gauze packing with much difficulty.

TABLE 1

R B C	4 660 000/c m m
Hemoglobin	14.1 gm %
W B C	6 750 c m m
Bleeding time	2-30"
Coagulation time	3'-30"
Platelets	302 520 c m m
Prothrombin time	32" (C A 96.9%)
Urea nitrogen	14.6 mg %
N P N	35 mg %
Sugar	93 mg %
carbon dioxide	50.4 mg %
Alk. phosphatase	22.4
Acid phosphatase	0
Kohn	Negative

There was a general oozing from the prostatic bed. No bleeding points were noted. The patient was returned to bed in poor condition but he responded to supportive measures. Brisk bleeding occurred when the packs were removed, it subsided spontaneously. Brisk bleeding also recurred on the thirteenth postoperative day but it again subsided spontaneously. In an effort to control the bleeding tendency protamine and synkavite were given without any appreciable effect. The patient made an excellent recovery after a prolonged hospitalization. His present condition and operative result are excellent.

Case 2. Mr. I. S. was a Negro 50 years of age. A transurethral resection of the prostate gland was performed 6 months before the enucleation. He continued to have a weak urinary stream and grossly infected urine. His bladder was irritable and he voided small amounts at frequent intervals. There was no residual urine. Cystoscopy revealed intra-urethral lateral prostatic lobes which met in the midline. The prostate gland was enlarged grade 2 on rectal examination. He was advised to have a suprapubic enucleation of the prostate gland. See table 2.

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pressure was at a safe level before the patient was removed from the operating room table. Medication did not seem to predispose to the bleeding.

DISCUSSION

Freedom from the painful ordeal of removing packs through the suprapubic wound is a remarkable benefit derived from the oxycel-bag technique. Our patients suffered much more when the packs were removed than they did during the immediate postoperative period. The prospects of having a second pack removed the following day was almost too much for many of them to bear. Morphine sulfate was given before the packs were removed but it was ineffective. General anesthesia was used in the latter years for the removal of the packs.

The risk of an additional anesthetic seemed appreciable. Nitrous oxide and oxygen was tried and was found unsatisfactory. Cyclopropine, which has the advantage of rapid induction and rapid recovery, seemed to predispose to excessive bleeding. Pentothal sodium and nitrous oxide with oxygen were the best.

TABLE 4

	XYCEL TECHNIQUE (50 CASES)	GAUZE PACKING (50 CASES)
1. Dry sinus	15.5 days	18 days
2. Erosions	None	7
3. Epididymitis	3	3
4. Thrombophlebitis	2	None
5. Osteitis pubis	1	None
6. Cystitis	1 (oxycel)	None
7. Deaths	1 (embolus)	2 (endocarditis) (shock)

agents but the severe stimulation engendered by removing the packs caused distressing laryngospasm on more than one occasion. Escape from the added risk of a second anesthetic came with the advent of the oxycel bag catheter technique.

Severe and persistent infection of the urine, which was a problem when the prosthetic bed was packed, has not been noted in the last 50 patients. The decrease in the amount of infection is also reflected in the minimal febrile reaction when the suprapubic sinus closes and the intravesical tension is re-established. Antibiotics were used prophylactically in both series of patients.

There have been few complications directly attributable to the oxycel-bag catheter technique. See table 4. Stress incontinence has been noted for a few weeks in 2 patients. Stockwell has written about incontinence that follows traction of more than 3 to 4 hours. We have not used tension. Early decompression of the bag diminishes pressure on the sphincters as well as actually inducing hemostasis. A nidus of oxycel which became impregnated with calcium salts was removed cystoscopically on one occasion. Ribi has written of a similar experience. The use of a single layer of oxycel instead of multiple layers around the bag has eliminated the aspiration of appreciable amounts of "jelled" oxycel and

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With the capsule thus incised sutures may also be placed at the lateral angles of the incision to aid in retraction and later closure. The prostatic adenoma is visualized through the capsular incision. It is freed by blunt and sharp dis-

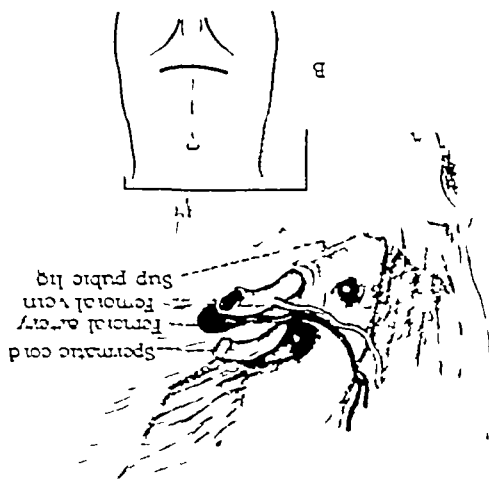


Fig. 3. Intrapelvic inguinal hernioplasty. Anatomic relationships as seen from perineal side are indicated. Asterisks mark site of direct and indirect inguinal hernias. Note in section of transversalis fascia into superior pubic ligament. Smaller figure indicates location of abdominal incision used. (After McVay and Anson, and Jennings, Anson and Wright.)



Fig. 4. Intrapelvic incision in hernioplasty. Placement of sutures for repair of direct hernia is in line of pubic tubercle and is continued laterally to femoral vein. Sutures may be placed as in *b* to aid in closure of abdominal inguinal ring, indicated in indirect hernias. (After McVay and Anson, and Jennings, Anson and Wright.)

tion the apex is mobilized by sharp division of the urethra. Dissection toward the bladder neck is aided by a rectal finger. The inferior vesical arteries are identified as they enter the prostate near the bladder neck and are ligated. Careful control of these vessels prevents excessive blood loss and maintains good visualization

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of the operative field. The adenomatous tissue is then freed from the vesical neck. A V-shaped portion may be excised from the posterior bladder neck to prevent later contraction. If the bladder neck is loose it can be sutured to the floor of the prostatic capsule. The cavity caused by removal of the adenoma is packed with a hot pack for 5 minutes, and after this time residual bleeders are controlled with forceps and electrocoagulation. A rectal finger will also aid in demonstrating residual tags and spheroids. A 24F Foley two-way irrigating catheter is introduced into the bladder through the urethra and the balloon distended within the bladder. In an occasional instance hemostatic agents such as oxycel or gelfoam are placed in the prostatic cavity during the closure. The capsule is sutured in 2 layers, the first is a continuous chromic catgut suture and the second is a series of interrupted sutures in which the hemostatic sutures placed prior to incising the capsule are utilized. This second row of sutures brings the prevesical and precapsular fat and fascia over the capsular incision. A soft rubber drain (Pen-rose) is inserted into the space of Retzius and brought out through a small stab wound just superior to the abdominal incision. If a hernia is present this is repaired prior to closure of the abdominal wall. The rectus muscles are brought together with 2 or 3 catgut sutures, the rectus fascia is closed with interrupted wire sutures with the knots directed into the muscle tissues, and the subcutaneous tissues and skin are closed with interrupted silk sutures. Closure is facilitated by readjusting the table to give a slight flexion at the hips. Routine vasectomies are carried out during the abdominal closure unless the patient objects to this precautionary procedure.

POSTOPERATIVE CARE

Following surgery continuous irrigation with normal saline solution or water is preferred for 24 hours or until the return remains clear. Antibiotics (penicillin or dihydrostreptomycin) are used routinely. Patients are allowed out of bed after the catheter has been removed. The postoperative course is smooth and uneventful. Bladder spasms are infrequent and morphine is unnecessary. The suprapubic drain is removed on the fourth postoperative day and the urethral catheter is removed on the fourth or fifth day. Voiding is usually satisfactory from the start.

HERNIA REPAIR

The hernia repair which can be effectively accomplished through the same incision is a superior pubic (Cooper's) ligament repair. The anatomy of this region has been clearly demonstrated by McVay and Anson who show that the posterior inguinal wall is a composite of the caudal portion of the transversus abdominis muscle aponeurosis and the investing fascia of this muscle. The fascia of the inner or peritoneal portion is the transversalis fascia. In the area where the muscle is aponeurotic these are fused. The transversus aponeurotic fibers contribute to the sheath of the rectus abdominis muscle anteriorly (in the inguinal area) and insert into the superior pubic ligament (Cooper's) as far lateral as the femoral ring (figs. 3 and 4). The transversalis fascia divides at the lateral margin of the rectus muscle to invest the rectus muscle and thus form the rectus fascia.

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Bitsch that in infectious process accounts for an excess amount of scar tissue with stricture. In addition it is our impression that the present latex Foley catheters appear to irritate and cause rapid contractions of preoperative urethral strictures. Epididymitis developed on the contralateral side (case 14) in a patient in whom only a unilateral vasectomy was done (A vasectomy was performed in 13 of the 14 patients.) One death in the early post-operative period (fourteenth day) was in a patient who previously had had a bilateral ureteral transplant and bilateral orchiectomy. He died at home and no post-mortem examination was obtained.

TABLE 1

CASE	PATIENT	AGE	GLAND	WEIGHT	POSTOPERATIVE DAY		COMPLICATIONS
					Catheter Removed	Home	
1	L S J	80	Ad *	157	5	22	Oxyeel gauze obstruction and infection
2	C G G	76	CA†	28	4	12	Urgency incontinence
3	B J C	73	Ad	51	5	13	
4	C E T	71	Ad	90	5	13	
5	R C	59	CA	170 + bladder	Ureteral trans- plants	8	Died at home 14th post op day
6	C I W	72	Ad	32	5	10	
7	I McC	83	CA		12	14	Urethral stricture
8	I S I	65	Ad	26	4	9	
9	M C S	79	Ad	130	4	10	
10	J C M	55	Ad	32	4	16	Residual tissue
11	W I J	60	Ad	120	5	16	Urethral stricture
12	I M I	57	Hernia repair only (illbus)		Small, infected		adenoma (Hem. staph)
13	I M	66	Ad	30	5	10	Urethral stricture
14	J V mS	73	Ad	24	5	15	Epididymitis (unilateral)
15	P J D	49	Hernia repair only		Small, infected		adenoma (tuberculosis)
16	B I	62	Ad	22	26	36	Post op bleeding (severe)

* Ad — Adenoma

† CA — Carcinoma

The transverse abdominal wounds healed without delay. We have found the transverse incision to be especially well adapted to the patient with an adipose abdominal wall (fig. 7). No incisional hernias and no untoward symptoms referable to the wounds have developed. In all cases there was only a minimal sero-sanguinous drainage from the stab wounds and these promptly healed with removal of the drains. Osteitis pubis has not occurred; we attribute this to careful hemostasis, avoidance of trauma to the periosteum of the pubis and absence of leakage from the prostatic capsule. No patients developed edema of the penis. There was only a low grade febrile response following retropubic prostatectomy. The highest elevation of temperature in most cases occurred on the first post-operative day (average 100.91°) and the temperature rapidly fell to normal by

was absent on one side and was decreased in size on the other. This small hernia has since been repaired by a Bassini procedure. Of the 4 patients with unilateral hernias, 1 patient had a vertical incision to avoid a large sliding hernia. This hernia has since been repaired by a conventional approach. In the other 3 patients with transverse incisions there has been an absence of hernias post-operatively in 2. The last 5 patients with hernias were subjected to a superior pubic (Cooper's) ligament repair as described previously. One patient had bilateral direct hernias. Only one side was repaired at the time of the retropubic prostatectomy, the opposite side has since been repaired by the Bassini method. Four hernias were unilateral, in 2 the hernias were indirect. In 3 there was an absence of hernia following surgery. An indirect hernia recurred in the fourth case, a patient who had had 3 previous herniotomies. The recurrence manifested itself 2 months after we had repaired the hernia through a transverse abdominal

TABLE 2 *Status of hernias following retropubic procedure*

Untreated hernias (6) Wound closure only

2 bilateral hernias (direct)

bilateral cure—1

unilateral cure—1 (R. side Bassini repair L. side later)

4 unilateral hernias (direct)

Hernia cure—2

Vertical incision—1

Treated hernias (5) Superior pubic ligament repair

1 bilateral hernia (direct)

R. intrapelvic repair—successful

L. Bassini repair later

4 unilateral hernias (2 indirect)

Hernia cured—3

Recurrence—1 (indirect)

Bassini repair later

incision. Examination during the fifth (conventional) repair revealed that insufficient sutures were placed during our fourth repair attempt. Tighter closure of the abdominal ring could have prevented this recurrence. It is still too early to accurately evaluate the results of these hernia repairs, but to date they appear to be solid and successful.

We have been favorably impressed with the retropubic operation for removal of the prostate. It provides an accessible method except in the presence of a very deep pelvis when a suprapubic enucleation may be preferable. The bladder and peritoneum remain undisturbed and this results in less trauma, shock and hemorrhage. Large adenomas can be removed by the retropubic method in one stage. Bacon reports the successful removal of an adenoma of 602 gm. Extra- and intracapsular hemorrhage can be controlled by the meticulous surgeon, and adenomatous tags removed under direct vision. The complications, not chargeable to the surgeon, are minimal. No special instruments were necessary to do the procedure. We have also found that a satisfactory hernia repair may be done

EVALUATION OF OXYCEL-BAG CATHETER TECHNIQUE IN SUPRAPUBIC PROSTATECTOMY

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It is proposed to set forth our clinical experiences with the use of oxycel and the bag catheter to control hemorrhage after suprapubic prostatectomy. The clinical histories of 100 private patients who were subjected to suprapubic enucleation of the prostate gland have been reviewed. The last 50 suprapubic enucleations of the prostate gland in which the older packing method was used are compared with the first 50 suprapubic prostatectomies in which the oxycel-bag catheter technique was used.

A brief description of our routine is presented. A single layer of oxycel is draped about the bag which is then distended partially with sterile water. The bag is drawn into the prostatic fossa and then it is further inflated with sterile water to fit snugly in the prostatic fossa. The bladder is closed in the routine manner around a 20F de Pezzer catheter which is placed high in the cystotomy wound. Tension on the distended bag may or may not be necessary. We have not used tension. Normal saline solution is used to determine the patency of the catheter. The catheters are not irrigated if they drain, regardless of the amount of bleeding. The bag is deflated 6 hours postoperatively if the drainage is not too bloody. The urethral catheter is removed 24 hours postoperatively. The suprapubic catheter remains until the tenth postoperative day. The suprapubic sinus is allowed to close spontaneously. If healing is slow, the closure is expedited by an indwelling urethral catheter which should keep the sinus dry from 48 to 72 hours.

Fifteen days was the average required to realize a dry suprapubic sinus and normal voiding when the prostatic bed was packed with gauze. An average of 14 days was required when the oxycel technique was used. This latter figure included two patients who required 42 and 36 days for closure. A transurethral resection of the bladder neck was necessary to correct the postoperative scarring in the first of the two patients. The second patient had exsanguinating primary and secondary hemorrhages.

in conjunction with a retropubic prostatectomy without an appreciable increase in morbidity. In such repairs an anatomic restoration of tissues is possible with utilization of the superior pubic ligament.

Functional results to date have been excellent. The postoperative sex function is undisturbed but can be improved with testosterone. Postoperative external ejaculation may remain absent due to incision or removal of the ejaculatory ducts proximal to the verumontanum (figs. 8 and 9).

CONCLUSIONS

A series of 14 retropubic prostatectomies were done, 11 for adenomatous hyperplasia and 3 for carcinoma of the prostate.

In these cases the functional results have been satisfactory.

Modifications in the technique of Millin which have been found beneficial are included. No special instruments were found necessary.

The transverse abdominal incision is of value in retropubic procedures and is especially adaptable to the obese abdomen.

An intrapelvic hernial repair may be accomplished following a prostatectomy and just prior to closure of the abdominal wound. Such a repair is anatomically sound.

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Penicillin 300 000 u streptomycin gm 1 and vitamin C 100 mg were given daily Morphine sulfate $\frac{1}{8}$ gr and scopolamine $\frac{1}{100}$ gr were given as pre-anesthetic medication The prostatectomy was done under pentothal sodium, nitrous oxide anesthesia This was supplemented with curare The prostate gland weighed 39 gm Bright bleeding was noted when the patient was returned to bed The bleeding persisted and the patient was returned to the operating room 8 hours after prostatectomy Arterial bleeding was noted and was controlled by fulguration The oxycel bag catheter technique was used again The remainder of the post-operative course was uneventful The functional result was excellent

Case 3: Mr B G was 70 years old Paget's disease of the bone was found on x-ray examination The patient had acute urinary retention for 4 days Catheter

TABLE 2

P. B. C.	4 300 000/c m m
Hemoglobin	11.4 gm %
W. B. C.	6 650/c m m
Bleeding time	2' 20"
Coagulation time	3'
Urea nitrogen	15 mg %
N. P. N.	32 mg %
Sugar	95 mg %
Carbon dioxide	57.9 vols

TABLE 3

P. B. C.	4 160 000/c m m
Hemoglobin	12.6 gm %
W. B. C.	12 400/c m m
Bleeding time	1' 30"
Coagulation time	2' 10"
Urea nitrogen	14.8 mg %
N. P. N.	34 mg %
Sugar	90 mg %
Carbon dioxide	57 vols %

ninth post-operative day. He was asymptomatic until 5 weeks after the operation when he developed pain down the anterior and medial aspects of both legs and in the groins. He walked with a stooped, shuffling gait and change of position was excruciatingly painful. Marked tenderness was present over the symphysis pubis and in the groins, and adductor spasm was conspicuous. These symptoms increased progressively until he was unable to leave his bed. He was treated symptomatically for 4 weeks at which time x-rays (fig. 1) were obtained (9 weeks post-operatively). The typical moth-eaten appearance of osteitis pubis was noted. He was hospitalized for 1 week during which time he ran a low grade fever. Roentgen therapy was administered as well as a 5 day course of streptomycin and penicillin with no immediate relief. The symptoms subsided gradually but it was not until 3½ months after the operation that the patient was free of pain and able to walk again.



FIG. 1 Case 1. Film 9 weeks after retropubic prostatectomy showing erosion of symphysis and pitted rarefaction of pubic bones.

Case 2. A 59-year-old man gave a history of a transurethral resection in September 1945. His symptoms recurred in June 1948. A retropubic prostatectomy was done on August 26, 1949. The urethral catheter was removed on the fifth post-operative day. Because of urinary leakage from the suprapubic wound, the urethral catheter was replaced for another 10 days, after which the wound healed and the patient voided spontaneously. He was asymptomatic for 6 weeks when pains developed on the outside of his legs and in the groins, and he experienced great difficulty in walking. The symptoms became progressively worse until the patient was confined to bed. Since he was no longer a resident of our city he sought treatment at another clinic where tuberculous was suspected because of the abnormal suggestive gait. X-rays taken at this time (8½ weeks post-operatively) were considered to be negative (fig. 2, A). A subsequent review of the same films show the fuzziness and erosion characteristic of the earliest signs of osteitis pubis. When he returned to our office 10½ weeks after the operation, he was able to walk with a straddling gait. At this time the films showed extensive changes in the pubic bones (fig. 2, B). Symptomatic and supportive

the danger of foreign body complications. An inflated bag in the prostatic bed will cause bladder spasms. This complication can be avoided by gently and partially distending the bag. The bag is deflated in 6 hours, which eliminates all pressure in the prostatic fossa.

The one death which occurred in the oxycel group was due to a massive embolus on the eighth postoperative day. This patient was an obese, white man 66 years old. His blood pressure preoperatively was 172 millimeters of mercury systolic and 106 millimeters of mercury diastolic and he had a tachycardia of 100 per minute. His electrocardiogram was within normal limits. The blood picture was normal. Two of the 50 patients who were packed after suprapubic prostatectomy died. One of these was a 72 year old white man, who had a marked systolic heart murmur. He died from bacterial endocarditis 19 days after surgery. The second patient was an obese white man, 64 years of age, who suffered severe shock after surgery and did not respond to the usual therapy. He died 48 hours postoperatively.

CONCLUSIONS

The oxycel-bag catheter technique is an improved method for control of hemorrhage after suprapubic enucleation of the prostate gland. There is a decrease in blood loss. There is a decrease in the amount of infection. The patient is more comfortable. There is shorter hospitalization.

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namely daily injections of solution B and diathermy treatments, but there was no significant improvement. The diagnosis of osteitis pubis was confirmed by films taken seven weeks postoperatively (fig. 3). Symptoms continued for a period of 2½ months when the pain began to ease.

COMMENT

Three cases of osteitis pubis out of 20 is indeed a high incidence. It is difficult to explain why some who have used this procedure have not encountered one case while other men have had this unfortunate complication several times. In the first case we believe that we nicked the periosteum with the point of the needle. In the second case the periosteum may have been injured by overzealous retraction. Up to this time a midline suprapubic incision had been used. We then changed to a transverse incision being careful to avoid any trauma to the periosteum. In the last case injury undoubtedly occurred in the search for the broken needle. It should be noted that the osteitis resulted in spite of the prophylactic use of penicillin and streptomycin. We are forced to conclude that the prevesical space is still one to be entered with a great deal of caution.

SUMMARY

Three cases of osteitis pubis are reported. These followed retropubic prostatectomy. The etiologic factors are unknown but trauma to the periosteum may have been the inciting cause. The diagnosis is simple if one keeps this complication in mind. The symptoms are suggestive and x-ray studies confirm the diagnosis. No specific treatment is indicated. Supportive and symptomatic therapy is all that may be offered. Fortunately the disease is self-limiting.

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muscle is divided in the plane of the skin incision and the muscles are retracted laterally. The space of Retzius is thus widely exposed. Careful blunt dissection just posterior to the symphysis pubis with manual traction on the bladder and peritoneum will open the space just anterior to the prostatic capsule (figs 5 and 6). Through the thin prevesical fascia the precapsular veins are visualized. These veins are ligated, divided with the fascia and pushed aside. This exposes



FIGURE 1. A—Normal bladder floor. B—Bladder floor consistent with hypertrophy of prostate.



FIGURE 2. A—Normal bladder floor.

FIGURE 2. B—Bladder floor consistent with hypertrophy of prostate.

A composite break-down of the various age groups and the methods of treatment are shown in table 1.

Conventional methods of prostatic surgery were used: transurethral (electrocautery resection), one-stage suprapubic, two-stage suprapubic, and perineal prostatectomy. Of the total number of 347 prostatectomies, 202 cases (58.2 per cent) were treated transurethrally. In most instances the Stern-McCarthy instrument was used. In recent years, the Nesbit instrument has become increasingly popular. None of our cases were treated by the cold-punch method.

Sixty-two cases (17.8 per cent) had a one-stage suprapubic operation. Of the remaining 24 per cent, 81 were two-stage suprapubic operations, and 2 cases were perineal prostatectomies. It is interesting to note that these 2 cases (0.7 per cent) did well although the total number of perineal prostatectomies attests to its unpopularity.

TABLE 1 Age and type of prostatectomy

AGE	TRANSURETHRAL	ONE STAGE	TWO STAGE	PERINEAL
Under 40 yrs	1	0	0	0
40 to 49 yrs	4	0	0	0
50 to 59 yrs	27	9	8	2
60 to 69 yrs	71	34	32	0
70 to 79 yrs	75	17	34	0
80 to 89 yrs	24	2	7	0

The incidence of carcinoma in this series of cases compares favorably with that of other investigators, namely, Lowsley and Kirwin,⁴ Vest,¹ and Treiger, Wolfeld and Mart.⁵ In the entire group of 368 cases I found a pathological diagnosis of carcinoma in 47 cases (13.45 per cent). The average age of those cases with carcinoma was 71.1 years, the youngest being 50 years, and the oldest 82 years. The age incidence is somewhat higher than the figures reported by Vest.¹

Thirty-two of the cases of carcinoma were treated by transurethral resection. The remaining 13 were treated by suprapubic enucleation, and the 2 cases of perineal prostatectomy were for carcinoma of the prostate. In those cases treated by methods other than transurethral resection and perineal prostatectomy the diagnosis of carcinoma was not made by the operator prior to the time of surgery.

In 3 of the cases of carcinoma of the prostate the patients died as a result of surgical intervention or during the immediate postoperative period, and 4 patients died following prostatectomy of metastases or as a result of carcinoma.

The selection of the anesthetic agent in this series was entirely in the hands of our department of anesthesia. Spinal anesthesia of one form or another was used in 290 cases (83.5 per cent). Intravenous sodium pentothal anesthesia was used in only 27 cases (7.7 per cent). The remaining 29 cases were operated on under some form of inhalation anesthesia. The limited use of the intravenous

⁴Lowsley, O. S. and Kirwin, T. J. *Clinical Urology*, Baltimore, Williams & Wilkins, 1944.

⁵Treiger, P., Wolfeld, J. and Mart, J. *Urol. & Cutan. Rev.* 52: 8, 1948.

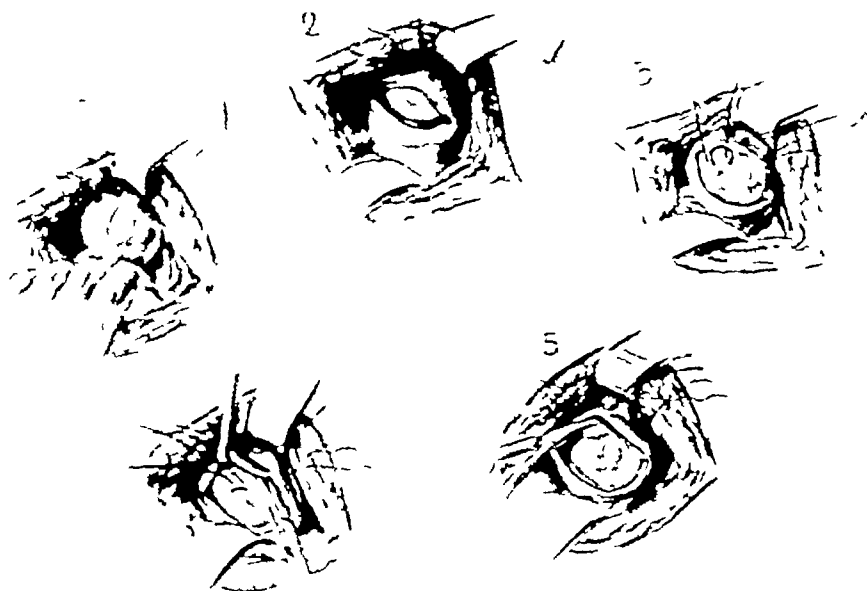


Fig. 7. Pre-clamp 1 for retroperitoneal prostatectomy. 1 Bladder and peritoneum are incised, revealing prostatic capsule. Hemostatic sutures placed about capsular area. 2 Prostatic capsule incised transversely proximal to hemostatic sutures. 3 Adenoma exposed through capsular incision. Double loop of heavy chromic catgut suture in adenoma. 4 Adenoma dissected from capsule of prostate by blunt and sharp dissection. 5 Adenoma removed by sharp division of urethra.



In group 1 of the major complications, 13 cases with 4 deaths were found. In group 2 there was a total of 26 cases and 16 deaths. The complications and the deaths from each are shown in table 2.

In the group of minor complications, the following were considered: 1) post-operative hemorrhage subsiding without intervention, and requiring less than

TABLE 3 *Individual causes of death*
Transurethral Resection

CASE NO.	AGE	DIAGNOSIS	TIME OF DEATH	CAUSE	AUTOPSY
47-9257	64	Carcinoma of Prostate	28 days	Metastases	No
47-503	81	Benign Hypertrophy	11 days	Uremia	No
47-809	89	Benign Hypertrophy	18 hrs.	Hemorrhage shock	No
47-6227	69	Benign Hypertrophy	3 hrs.	Septicemia coronary	Yes
47-1167	64	Carcinoma of Prostate	3 days	Aerogenes septicemia	Yes
44-6333	78	Benign Hypertrophy	6 hrs.	Pulmonary embolus	No
43-2570	59	Benign Hypertrophy	40 days	Coronary clot of lung	Yes
45-1219	75	Benign Hypertrophy	9 days	Hemorrhage uremia	No
45-6318	69	Benign Hypertrophy	9 days	Septicemia	No
48-1133	81	Benign Hypertrophy	3 hrs.	Explosion and bladder rupture	Yes
47-6227	69	Benign Hypertrophy	3 days	Septicemia	No
<i>One Stage Suprapubic Prostatectomy</i>					
47-5309	69	Benign Hypertrophy	2 hrs.	Embolus pulmonary	No
39-976	60	Benign Hypertrophy	6 days	Septicemia perinephric abscess	Yes
48-4242	72	Benign Hypertrophy	22 days	Coronary	No
48-8474	62	Carcinoma of Prostate	3 days	Congestive heart failure	No
<i>Two stage Suprapubic Prostatectomy</i>					
47-7420	88	Benign Hypertrophy	26 days	Hemorrhage septicemia	Yes
45-8417	74	Benign Hypertrophy	8 days	Hemorrhage coronary	No
44-6238	69	Benign Hypertrophy	58 days	Septicemia hemorrhage	Yes
41-1917	59	Benign Hypertrophy	6 days	Septicemia	No
42-6885	79	Benign Hypertrophy	56 days	Coronary	No

Carcinoma of lung primary cause of death

one unit of blood as replacement; 2) chills and fever in excess of 101°F, and with negative blood culture; 3) pulmonary atelectasis responding to treatment; 4) acute and chronic epididymitis; 5) others.

Of the 59 cases in the group of minor complications, 20 patients (5.7 per cent) developed postoperative epididymitis. All developed in the absence of vas ligation.

The total number of deaths in this series has been mentioned under post-operative complications. A further study reveals that there were 11 deaths in the 202 transurethral resection (5.4 per cent), 4 deaths in 62 one-stage suprapubic prostatectomies (6.4 per cent), and 6 deaths in 51 two-stage suprapubic

Purposeful repair of inguinal hernias during the course of a retropublic prostatectomy is similar to the McVay procedure in that the superior pubic ligament is utilized. McDonald and Huggins have done a simultaneous prostatectomy and inguinal hernia repair but have utilized separate incisions and a Bassini or Halsted type of repair. The transversalis fascia is sutured to the superior pubic ligament from the pubic tubercle to the femoral vein (figs. 3 and 4). Inferior epigastric vessels will usually not have to be divided in order to accomplish this. If the abdominal inguinal ring is not closed snugly about the spermatic cord closure can be further accomplished by placing sutures in the fascia just lateral to the abdominal inguinal ring as advocated by Jennings, Anson and Wright. Repair of a hernia can be satisfactorily accomplished by this method whether the hernia is of direct, indirect or combined types. If an indirect hernia is encountered the sac is opened and the contents reduced into the abdominal cavity. A high ligation of the sac is easily accomplished. If the distal portion of the sac extruding into the inguinal canal or scrotum is not reducible it may be left in place. Should the transversalis fascia be of poor structure a fascial graft may be utilized.

DISCUSSION

Upon admission to the hospital all patients had symptoms of progressive prostatic obstruction which were variable in degree and in duration. Three were admitted with acute urinary retention (cases 1, 3, 11, table 1). In 3 patients (cases 2, 5, 7) a previous diagnosis of carcinoma had been made, and in one of these (case 5) bilateral orchiectomies and bilateral ureteral transplants were accomplished previous to admission for a retropublic radical prostatectomy. In all cases the patients were considered as suitable surgical risks. The average blood urea nitrogen determination was 18.4 mg. per cent, the highest value being 28.6 (case 13). In two patients a retropublic prostatectomy was planned but was not accomplished because of the small fibrotic glands encountered, in addition the 2 patients had urinary tract infections somewhat refractive to treatment. One of these later subjected to a transurethral resection, the postoperative urine showed numerous and fast bacilli. A total of 14 retropublic prostatectomies were performed. 11 were for adenomatous hyperplasia and 3 were radical procedures for carcinoma. The tissue removed varied from 22 to 157 gm. with an average weight of 62 gm. Pertinent data are included in table 1.

OVARIAN CYST AND UREMIA

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Varying degrees of ureteral obstruction and upper urinary tract dilatation have been observed complicating many gynecological disorders. The most frequently noted of these conditions is carcinoma of the cervix, but ureterectasis and pyelectasis have repeatedly been observed in other pelvic malignancies, in such conditions as pregnancy, prolapse of the uterus, and endometriosis, and following pelvic radiation. A less commonly noted cause of ureteral obstruction is found in the benign pelvic neoplasms.

Though few cases of urinary obstruction due to benign ovarian cysts are reported in the literature, these are found in statistical series which indicate it to be a frequent occurrence.

Long and Montgomery¹ reported involvement of the urinary tract in 11 of 19 of their cases of ovarian cyst. Everett and Sturgis² found bilateral partial ureteral obstruction in 2 of their 5 cases and one of these also had urethral obstruction with bladder dilatation. Krietschmer and Kinter³ noted upper urinary ectasia in 51.9 per cent of their series of 11 ovarian cysts. Montgomery⁴ also reported 4 cases of ovarian cysts of which 3 were complicated by partial ureteral obstruction and hydronephrosis.

The number of reported cases is small, but the percentage of urinary tract involvement in all these series is high. The renal complication is almost always silent, and consequently the gynecologic lesion occupies the center of attention.

In all cases studied by pyelograms pre- and postoperatively, the obstructive phenomena rapidly regressed to normal or near normal following the removal of the pressure by resection of the cyst. Consequently, since the urinary tract disease is silent and regresses spontaneously after the obstruction is relieved, one might surmise that urinary obstruction is present but goes unnoticed in a high percentage of ovarian cysts.

In all of the foregoing mentioned cases, the urinary tract disease was discovered secondarily in working up cases with gynecological complaints. I was able to find but 1 case in the literature in which uremia had developed secondary to urinary obstruction by an ovarian cyst.⁵ I recently saw a woman who was admitted because of severe acidosis and uremia which developed from urethral and ureteral obstruction by a huge ovarian cyst.

CASE REPORT

A 54-year-old stuporous Hawaiian Caucasian woman was admitted to the medical service of the St. Francis Hospital November 28, 1950. No history

¹ Long J. P. and Montgomery J. B. *Am J Obst. & Gyn.* 59: 552, 1950.

² Everett H. S. and Sturgis W. J. *Urol. & Cutan. Rev.* 44: 638, 1940.

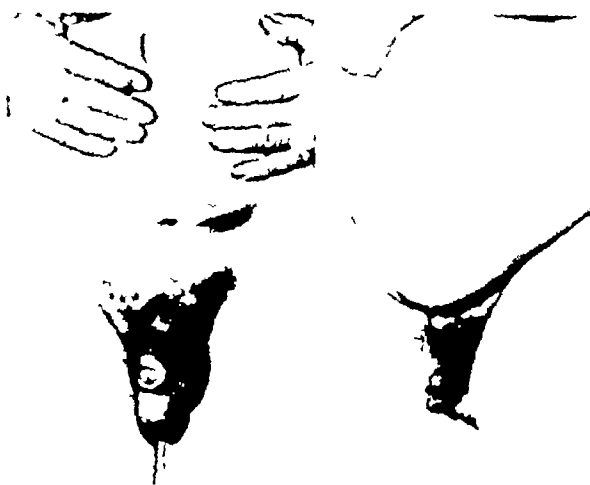
³ Krietschmer H. I. and Kinter A. I. *J. A. M. A.* 109: 1097, 1937.

⁴ Montgomery J. B. *Penn. Med. J.* 47: 1080, 1944.

⁵ Borras P. I. and Loza P. G. *Rev. Assoc. Med. Argent.* 60: 244, 1946.

the third or fourth day. The hospital stay following surgery averaged 15 days. The longest period was 36 days in a patient (case 16) who had recurrent severe post-operative bleeding.

Following the use of the transverse abdominal incision (only 1 vertical incision in the series) we noted a satisfactory repair of inguinal hernias in some patients. One patient who had worn a bilateral truss for 35 years stated he no longer needed this protection. Another patient had a small right direct hernia which disappeared after retropubic prostatectomy through a transverse incision. Examination almost a year following surgery confirms the apparent disappearance of the hernia. In earlier cases in which the transverse abdominal incision was utilized the rectus abdominus muscles were divided transversely as an aid in exposure. In repairing the operative wound these divided muscles were reapproxi-



performed on January 13, 1951, by Dr. James Wong. A tremendous multi-loculated cystic tumor of the right ovary was removed and found to be filled with serous fluid. Microscopic examination of multiple areas of the neoplasm showed a serous cystadenoma with no evidence of malignancy.

The patient had a relatively uneventful convalescence. The fecal incontinence gradually improved and finally disappeared, the nonprotein nitrogen fell to 45 mg. per cent and excretory urograms taken 4 weeks after surgery revealed excellent concentration and excretion of the dye and almost complete regression of the dilatation of the ureters and renal pelvis (fig. 1, C).

COMMENT

This case is unusual in that the condition which brought the patient to the hospital was renal insufficiency, rather than the tremendous mass of the cyst itself. The remarkable return of function and anatomical normalcy of the ureters and kidneys incident to the removal of the cyst is also noteworthy in view of the advanced changes and almost complete lack of function seen when the patient first came under our observation.

The paucity of case reports noting urinary involvement in ovarian cysts would seem to indicate that knowledge of its possible occurrence is not widespread and it suggests the recommendation that an excretory urogram would be a worthwhile preoperative study in all such cases.



FIG. 8. Gross specimen of prostatic tissue with contained ejaculatory ducts

no positive evidence. In accordance with the general consensus of opinion of today (Borthwick, Medlar and others) that epididymitis is always caused by ductal spread from the pelvic genitalia, it may be assumed that tuberculosis of the prostate or of the seminal vesicles was present also in these 4 patients. Evidence of genital tuberculosis was absent in 2 cases only, in 1 case no information of the pelvic genitalia is available.

A fact suggesting that the tubercle bacilli were referable to the pelvic genitalia was that the urine specimens used for guinea-pig inoculation were always taken after previous expression of the prostate gland. In some cases, in which control tests were made of specimens of urine taken without previous expression of the prostate, guinea-pig inoculation gave a negative result.

TABLE 1 *Results of a re-examination carried out 1946-1948 of 201 patients nephrectomized during the years 1934 to 1943 for renal tuberculosis at the General Hospitals of Stockholm*

	MEN	WOMEN
No. patients	112	89
Deaths	31 (28 p.c.)	13 (15 p.c.)
Re-examined		
Guinea pig tests pos.	34	5
Guinea pig test neg.	40	60
Guinea pig test not made	1	1
Healthy (according to patient's written report)	3	4
Not traceable	3	3

TABLE 2 *Interval between nephrectomy and guinea pig tests with the urine of the males*

YEARS AFTER NEPHRECTOMY	POS. GUINEA PIG TEST	NEG. GUINEA PIG TEST
3-5	10	15
5-7	8	11
7-10	9	8
10-14	7	6

Genito-urinary tuberculosis could not even be regarded as healed in all of the 10 males where the guinea pig test of the urine was negative, because a) several of them showed evidence of tuberculous foci in the prostate or in the seminal vesicles which foci might of course have healed in some of the cases, b) 5 of them showed signs of epididymitis and c) in 3 there were fistulas after recent epididymectomy. Seven of them had bladder symptoms which might possibly have been nonspecific in some cases.

Hence judging by this re-examination carried out 3 to 14 years after nephrectomy genito-urinary tuberculosis was cured in only about one third of the men—a result which does not seem to be much better than the follow-up investigation presented in Sweden in 1925 by Lundberg, Persson and others. This means then that we have come to the same conclusion as Ix and others, namely that our endeavors to improve the result of our treatment of renal tuberculosis by early diagnosis and early operation have not been rewarded by the success anticipated.

The reason for this disappointment is apparently that we surgeons used to

OSTEITIS PUBIS FOLLOWING RETROPUBIC PROSTATECTOMY

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Since its introduction in this country by Terrence Millin in 1946, retropubic prostatectomy has been given a wide trial. Sufficient time has elapsed to permit one to draw definite impressions as to mortality rate, complications and end results. From a limited experience with 20 cases, retropubic prostatectomy was found to have many advantages, namely, it is easy to learn, it is a visual procedure, control of hemorrhage is about equal to that in perineal prostatectomy, and the patients are quite comfortable in the postoperative course. The disadvantages, which we have noted are: 1) the difficulty of adequate exposure in obese individuals; 2) the persistence of small amounts of residual urine and pyuria. In one case in which a wedge-shaped piece of tissue had been removed from the posterior lip of the bladder neck, additional tissue had to be removed transurethrally at a later date because of the persistent residual urine and pyuria. Probably the amount of tissue removed at the initial operation was inadequate. 3) The most disheartening feature, however, was the occurrence of 3 cases of osteitis pubis, and this has caused us to abandon the procedure for the present.

Edwin Beer first described osteitis pubis in 1924. Muschat, in 1945, was able to collect 25 cases from the literature, including two of his own. Since 1945 we have been able to find another 35, including the 3 which we are reporting. The actual number must be much greater because in talking to urologists at the various meetings we know of individual cases which have not been reported. It will be noted that the figures show a marked increase in the incidence of this complication, and this is all the more striking when we realize that it has occurred in the

UNILATERAL PYELONEPHRITIS ACCOMPANIED BY HYPERTENSION, RELIEVED BY NEPHRECTOMY

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Goldblatt¹ created much interest in the relationship between generalized hypertensive vascular disease and unilateral renal disorders by demonstrating an elevation in blood pressure following constriction of one renal artery with a silver clamp. He later observed that hypertension following renal ischemia immediately returned to normal after removal of the affected kidney.

Gasul et al.² recently reviewed the literature and found only 31 cases of hypertension corrected by nephrectomy. Nine of the cases were children and in 8 of these the hypertension was associated with unilateral pyelonephritis.

The case reported here is one of advanced unilateral pyelonephritis accompanied by hypertension which was corrected by nephrectomy.

CASE REPORT

Mrs. K. K., a white woman, aged 27, was first seen on May 21, 1948, complaining of high blood pressure, nervousness with tightness in her chest, loss of appetite and episodes of nausea and vomiting when food was forced. She had known of her hypertension since her first pregnancy 9 years previously and had been informed then that the elevation in blood pressure was due to toxemia of pregnancy. She lost the child following premature delivery at 7½ months. Her second pregnancy was interrupted at 8 months by cesarian operation because of elevation of blood pressure, nausea, vomiting and general toxemia. At operation a portion of both fallopian tubes was removed for the purpose of sterilization. She was 19 years of age at this time.

During the following years the patient visited many doctors and clinics because of her hypertension which caused her great anxiety because her father had suffered with angina pectoris and had died suddenly with a heart attack at 43 years of age and she feared that her high blood pressure was leading her to the same end. She was advised by some physicians to have a sympathectomy for relief of her hypertension and was also told that one kidney did not function as well as the other but that there were no remedial measures to be undertaken.

The past history was irrelevant except for a severe and persistent sore throat for several weeks at the age of two or three. This was followed by an unexplained elevation of temperature and general debility for a number of months. The patient stated that her mother had always regarded her as being in poor health during childhood.

The patient displayed great anxiety about herself. She weighed 117 pounds and was 5 feet 3 inches in height. The skin was a little dry but her hair and nails were of good texture. The pupils were normal and reacted equally to light and

¹Goldblatt, H., Lynch, G., Hanzel, R. L. and Summerville, W. W. *Am. J. Path.*, 9, 912, 1953.

²Goldblatt, H. et al. *J. Exp. Med.*, 59, 347, 1954.

³Gasul, B. M., Gasul, J. M. and Crossman, A. *J. A. M. A.*, 139, 705, 1949.

treatment resulted in gradual improvement and spontaneous cure and the patient was able to walk 15 weeks after surgery and 10 weeks after onset of pain.

Case 2. A 72 year old man had purulent urine and catheter drainage for several weeks before a retropubic prostatectomy was done on April 19, 1949. In closing the capsule a needle was broken and one fragment could not be found.



FIG. 2. *Case 2.* A film taken 8½ weeks postoperative showing fuzziness and early rarefactions of symphysis pubis. B 10½ weeks postoperative showing progression of lesion.



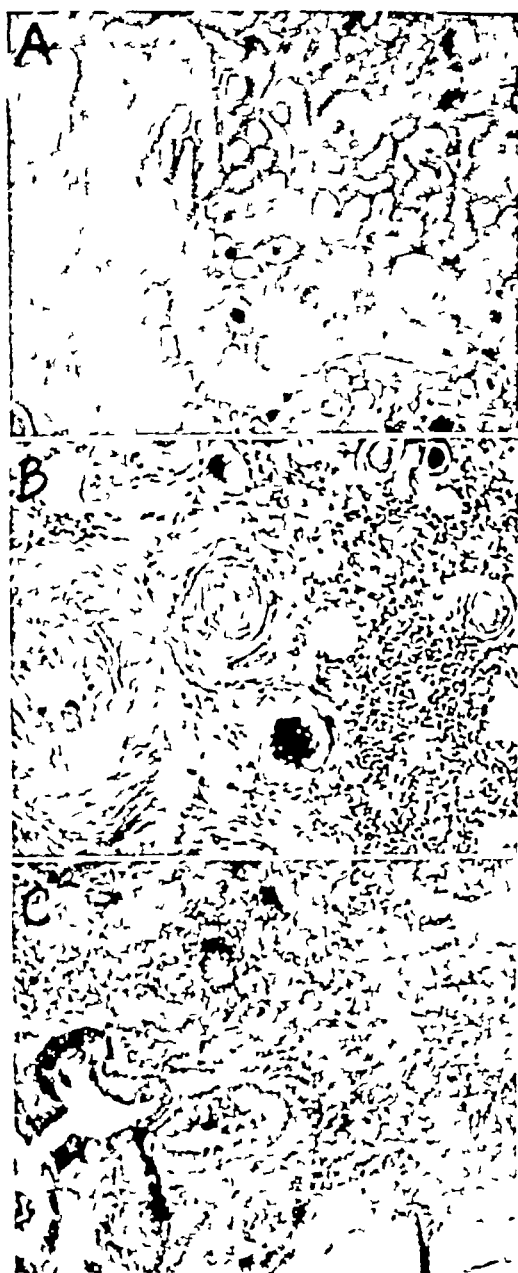


FIGURE 2

ureter measuring 6 cm. and contained a small stone in the lower calyx measuring approximately 5 by 3 mm. The capsule stripped with difficulty leaving a pale reddish to light tan cortical surface through which were scattered large light colored fibrous arcs. On cut section the cortex measured less than 1 mm

There was a rapid weight gain of 19 pounds in 7 months. Her general nervous status changed from one of anxiety to confidence. It might be considered that her psychic overliability had been corrected by doing something to her in the magnitude of a major operation, but the fact remains that a badly diseased and practically nonfunctioning kidney was removed.

SUMMARY

A case of hypertension with unilateral pyelonephritis relieved by nephrectomy is reported.

It is quite possible the unilateral kidney disease dates from severe and prolonged tonsillitis at 2 years of age.

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type of anesthesia is due to the unpopularity of this type of anesthetic in our department of anesthesia.

In order that an accurate evaluation might be made of the relationship that exists between the various methods of prostatectomy and the hospital stay, it is necessary to consider not only the total number of hospital days, but the number of postoperative days as well. This is essential since the diagnostic work up and preparation prior to surgery vary with the patient and the attending physician.

The average hospital stay for those operated on by the transurethral route is 24 days with a postoperative period of 14.2 days.

In the group managed by the one-stage suprapubic operation the total stay averaged 25 days with a postoperative period of 21 days. The two-stage prostatectomies remained in the hospital for a total of 52 days, with a postoperative period of 34.2 days.

TABLE 2 *Causes of complications and the deaths*

CAUSE	NO. CASES	DEATHS
Hemorrhage alone	9	3
Hemorrhage with uremia	2	1
Hemorrhage with hypotension	1	1
Hemorrhage with coagulopathy	1	0
Septicemia with coagulopathy	2	2
Septicemia alone	10	6
Cardiac failure	5	4
Cardiac failure with pulmonary embolism	2	1
Pulmonary embolism alone	2	1
Complications of anesthesia	1	0
Unexplained	2	0
Unexplained death	2	2

with a duodenal fistula after nephrectomy there is an increase in nitrogenous wastes due to caloric restriction and autogenous tissue consumption. Only one kidney remains and its function may be impaired by pre-existing disease. Therefore, it is necessary to maintain a urinary output of 1,500 ml to reduce the renal effort in clearing the waste products.

TYPES OF DUODENAL FISTULAS

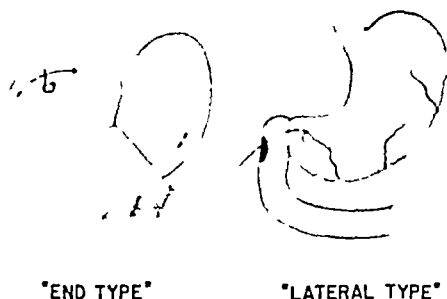


FIG. 1

TABLE 1. Secretions of upper gastro intestinal tract in 24 hours

Salivary	1,500 ml
Gastric	2,500 ml
Biliary	500 ml
Pancreatic	700 ml
Total	5,200 ml

COMPOSITION OF PLASMA

IN MILLIEQUIVALENTS PER LITER

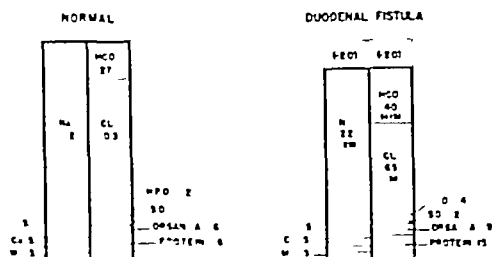


FIG. 2. Depicting composition of plasma in normal and in patient with duodenal fistula. Note hypochloremia and alkalosis, increase in organic acids, phosphate, and sulfate. Relative increase in protein fraction occurs as a result of dehydration.

The electrolyte content of the fluid lost through the fistula varies in a single patient so that no hard and fast rule can be made concerning replacement. If one-half of the volume lost is supplied as normal saline and one-half is 5 per cent glucose in water, relatively accurate replacement is being made.

One to 2 gm of potassium chloride must be supplied for each liter of fistula

prostatectomies (7.1 per cent). No deaths occurred in the 2 perineal prostatectomies.

Again referring to Melick's figures on mortality in this same hospital in 1943, we find a mortality of 15.4 per cent for the one-stage suprapubic operation and 6.6 per cent mortality for the two-stage operation. The correlation between these figures and the extensive use of antibiotics and chemotherapy in recent years must be considered.

The 21 cases in which death occurred are reviewed briefly in table 3.

SUMMARY

A series of 347 consecutive prostatectomies from one private hospital, done by 6 staff urologists over the past 10 years has been reported.

The statistics on hospital stay and postoperative stay averaged 24 days and 14.2 days for the transurethral operation, 25 days and 21 days for the one-stage suprapubic operation, 52 days and 34.2 days for the two-stage suprapubic prostatectomy, 31 and 28 days for the perineal prostatectomy.

Transurethral prostatectomy was the method of choice in the majority of cases, regardless of age of the patient.

The mortality rate and hospital stay were less with transurethral resection than with any other method.

A sufficient number of cases of suprapubic prostatectomy are still being done to indicate that it is the procedure of choice in selected cases.

A comparison of mortality figures reported at this hospital before and after the introduction of antibiotics is made, and showing a lowering of the one-stage suprapubic mortality, but the antibiotics have not influenced the mortality of the two-stage suprapubic.

There has been little or no appreciable change in the hospital stay of suprapubic prostatectomies.

caloric intake is provided. The fistula drainage may be re-fed into the jejunum and thus obviate the problem of electrolyte loss.

Adequate nutrition results in improvement in the patient's condition and the fistula will usually close. If the fistula fails to close the patient will be in fit condition for operative repair of the fistula.

OPERATIVE MEASURES

The available operations for duodenal fistula are listed in table 3. A feeding jejunostomy is indicated in the event a double lumen intestinal tube can not be passed distal to the fistula or is not tolerated well. If provided in the early case it will prevent the malnutrition which is certain to occur. In the late case, jejunal feedings are a satisfactory method of correcting the malnutrition which has occurred.

Early repair of the fistula even when combined with a gastrojejunostomy, is doomed to failure inasmuch as the duodenal wall is too friable to withstand the intraduodenal pressure, particularly in a depleted patient.¹¹

Excision and closure combined with gastrojejunostomy and duodenal occlusion or interruption is theoretically an adequate operation but in practice it

TABLE 3 Available operations for duodenal fistula

- 1) Feeding jejunostomy
 - Good early—maintenance of nutrition
 - Good late—nutritional recovery
- 2) Gastrojejunostomy and closure of fistula early
 - Inadequate operation
- 3) Gastrojejunostomy, fistula repair and duodenal interruption
 - Adequate operation
 - Prohibitive mortality—85%
- 4) Excision and closure of fistula or more complex procedures
 - Only for fistula persistent after general improvement

is an extensive procedure for a poor risk patient. The reported mortality is 85 per cent.¹

The operative treatment of duodenal fistula then is limited to certain specific indications: 1) jejunostomy when necessary to provide additional nutrition; 2) direct operative attack when the fistula persists despite general improvement in the patient's condition with conservative treatment. These considerations are illustrated by the following case.

REPORT OF CASE

A 42-year-old Negress who had had a right thorico-plasty in 1936 entered the hospital in June 1950 with a chief complaint of right flank pain, chills and fever. A diagnosis of right staghorn calculus with pyonephrosis was subsequently made. A right nephrectomy was performed June 29, 1950. At operation because of chronic perinephritis the kidney was firmly adherent to the surrounding structures. Inspection of the wound after the kidney had been removed

¹ Moore: *Re Abdominal Operations*. New York: Appleton Century Crofts, 1948, chap. 11.

¹¹ Colp: *Ann Surg.* 78:725-744, 1923.

is available. Blood pressure was 140/90, pulse 110 per minute, temperature 100 $\frac{1}{10}$. She was markedly dehydrated. The abdomen was huge and contained three basketball-sized masses which seemed to arise out of the pelvis and reached to the costal margins. Neither pelvic nor rectal examinations could be done because the cystic masses prevented the introduction of a finger into either the rectum or the vagina. She was incontinent of both feces and urine.

Blood nonprotein nitrogen at the time of admission was 200 mg. per cent and CO₂ combining power (11 volumes per cent) revealed a marked acidosis. Catheterization was very difficult because the urethra was compressed against the posterior surface of the symphysis, but when it was accomplished 1 liter of foul cloudy urine was obtained and the centermost of the three abdominal masses disappeared.



FIG. 1. *A*, excretory urograms immediately after admission revealing no appreciable function of the kidneys. *B*, retrograde pyelogram, contrast medium clearly on right side of film. *B*, retrograde pyelogram, contrast medium on left side of film, showing lateral displacement of left ureter and elongation and dilatation of ureters. *C*, excretory urograms, contrast medium well marked ureterectasis and pyelectasis. *C*, excretory urograms, contrast medium well marked ureterectasis and pyelectasis. *C*, excretory urograms, contrast medium well marked ureterectasis and pyelectasis. *C*, excretory urograms, contrast medium well marked ureterectasis and pyelectasis.

mentary parenteral feedings. During the fifth week a "feeding" jejunostomy was provided. Following this, improvement was gradual but definite. In the sixth week drainage increased and it was noted on x-ray examination that the suction catheter had migrated through the fistula into the duodenum. The catheter was removed and the drainage decreased in amount until it was minimal. 3 weeks later, that is, 9 weeks after operation.

The course of the patient is illustrated in figure 4. On the twentieth day the fistula drainage was over 2,000 ml daily. The intake had been allowed to drop, the urine output decreased to 700 ml, the plasma chlorides fell, there was a compensatory rise in the CO_2 combining power. The patient was dehydrated and had a hypochloremia, a hypopotassemia, and an alkalosis. This was corrected by the observance of the rules for replacement therapy. One thousand milliliters of water was supplied for insensible loss, 1,500 ml for urinary output and 2,000 ml, one-half of which was saline, for the fistula drainage. The calculated potassium loss was replaced.

SUMMARY

The active urologist who performs right renal operations will encounter duodenal fistula a most distressing complication.

Massive fluid and electrolyte loss and enzymatic tissue digestion occur in a patient with a duodenal fistula. The untreated patient dies of starvation, dehydration, alkalosis and uremia.

The patient's best chance for recovery lies in 1) the maintenance of fluid and electrolyte balance, 2) the maintenance of optimal nutrition, and 3) the prevention of tissue digestion.

Direct operative attack to close the fistula is reserved only for the patient whose fistula fails to close after vigorous application of the conservative plan.

to the bladder would be reasonably straight. The suture line in the area of anastomosis must not be under any tension. Great care must be exercised in the preservation of the blood supply of the ureter, this is especially true when large portions of the distal end have to be resected. It has been our experience that along the mid course of the ureter, especially on the left side, a large blood vessel is present arising out of the common iliac artery or the hypogastric artery and coursing retroperitoneally to reach the ureter. We have aimed, whenever possible, at the preservation of this blood vessel, especially when the area to be resected was proximal to it, as its presence insures a good blood supply to the lower segment.

In the first group of cases two procedures were tried: the first, the transverse section of the ureter and end-to-end anastomosis, the second, the elliptical spatulate end-to-end anastomosis as advocated by Nesbit. Sutures used in both methods were identical and, as in arterial surgery, the margins of the ureteral segments were carefully approximated by interrupted mattress sutures of 0000 chromic catgut in such a way as to evert the edges. If the lower segment of the ureter below the stricture is of normal size and the proximal segment above the stricture is greatly dilated, an end-to-end anastomosis is technically very difficult. This can be partially corrected by the removal of a narrow, longitudinal strip from the upper segment for a distance of 1½ inches, and suturing the two sides together by interrupted mattress sutures until the size of the ureter approximates that of the lower segment. In spite of this, the technical difficulty is great and probably leakage at this site accounts for some of the failures that were encountered by this method. Patients were examined regularly in the postoperative period for several months to ascertain the condition of the anastomosis and the amount of constriction at the site of the sutures, the development of hydronephrosis above, and function of the ureter following each of the procedures used.

In the assessment of the final end result in any given case the result "good" was applied to those cases which had no constriction at the site of anastomosis as proved by cystoscopy and retrograde catheterization, whose hydronephrosis and kidney function had improved as compared to the preoperative pictures, and whose infection had subsided. Under the term "fair" were those cases that had no constriction at the site of anastomosis but whose hydronephrosis did not improve or whose infection was still active, the last probably due to some defect in the mechanics of the ureter. In those cases classed under "failure" constriction had developed at the site of anastomosis and hydronephrosis and infection were more severe than preoperatively.

Three cases were first tried without the use of a splinting catheter, in the first group anastomosed end to end after transverse section. These 3 cases very quickly in the postoperative period met with disaster from fibrous constriction at the site of the anastomosis and finally had to undergo either secondary repair at this site or nephrectomy. The use of a splinting catheter after transverse section and end to end anastomosis was then tried in a group of 4 cases. Of these 4 cases 3 eventually developed complications from a constriction at the site of the anastomosis. 1 patient died from uremia 9 months later, 1 patient was

concentrate on or restrict our attention to the tuberculosis of the kidney, which is considered as a local disease and not as a local manifestation of a generalized infection or general tuberculosis. It is accordingly necessary that the surgical treatment be combined with medical and hygienic treatment, i.e. a sanatorium regimen. The importance of such treatment has increased since the introduction of various chemotherapeutic agents for combating the tuberculous infection.

We must discard the doctrine of the famous French urologist Albarrans (*abandonner le rein - néphrectomie immédiate*) and go over to an individual treatment of the renal tuberculosis and to postpone operation until the tuberculous infection is in a more quiescent or less active stage, *néphrectomie opportune* (de Brantomé).

Therefore nowadays we never operate for urogenital tuberculosis until the patient has been given sanatorium treatment with chemotherapeutics, mainly PAS—sometimes in combination with nephrochaulmoogreol, streptomycin and recently also with the German preparation Conteben (IB I 698 Domagk). Conteben seems to be very suitable for the local treatment of tuberculosis of the prostate. All patients are given the same postoperative treatment and we intend to keep them under observation at the sanatorium until the guinea-pig test of the urine is negative and we can hope the tuberculosis to be healed.

Our patients receive this sanatorium care in a recently established genitourinary tuberculosis service at Rylands Sanatorium situated 40 km. from Copenhagen. All examinations and operations are carried out at the surgical department of which is consulting urologist to the sanatorium.

A third sanatorium treatment is also given to a number of patients with bilateral renal tuberculosis (tuberculosis in the remaining kidney after nephrectomy) — patients only slightly amenable to the treatment earlier but who can now derive considerable benefit.

tions from 6 months to a year only one failure was detected. Three cases were classed fair and 8 good. Not enough evidence has accumulated to show that there is a real advantage in not using a splinting catheter. Our clinical impression is that patients are easier in the immediate postoperative period with a splinting catheter, but that in these same cases it takes longer for the infection to subside. See table 1.

For those lesions occupying the distal end of the ureter two methods were tried. In the first method after resection of the diseased portion of the ureter the ureter was split to a distance of half an inch, thus leaving two flaps. A catgut suture was then passed through each flap at its edge, and the ureter was passed into the bladder through the original ureteral orifice after very careful excision of all layers of muscle around the diseased ureteral orifice. The insertion of the distal end of the ureter to the bladder was always done through the original ureteral orifice after careful excision of all the muscular layers of the bladder immediately around the orifice. We have chosen this method rather than anastomosing the ureter higher up in the bladder because of the facility it provides

TABLE 1 *Group 1. Anastomosis of ureteral ends after resection of diseased portion*

PROCEDURE	NO. OF CASES OPERATED ON	GOOD END RESULT	FAIR END RESULT	FAILURE
Transverse end to end anastomosis. No splinting catheter used	3	0	0	3
Transverse end to end anastomosis using splinting catheter	4	0	1	3
Elliptical end to end anastomosis without use of splinting catheter	5	4	1	0
Elliptical end to end anastomosis with use of splinting catheter	7	4	2	1

for retrograde catheterization and dilatation. The flaps were then fixed to the bladder mucosa by fine catgut 0000 sutures, and two anchoring sutures were placed between the bladder musculature and the ureteral wall extravesically. A small incision was then made above the site of anastomosis and a T tube inserted, the lower arm of which would go beyond the anastomosis into the bladder. Six cases were operated on in like manner. Two cases showed good end results within 6 weeks of operation. One case was classed fair. There were 3 failures. 1 patient developed a urinary sinus at the site of anastomosis and refused further treatment. 1 patient developed hydronephrosis and had to be reoperated on at the site of stricture, and 1 patient developed hydronephrosis and had to undergo nephrectomy.

In the other method used, the upper end of the ureter was prepared for elliptical spatula end to end anastomosis after the resection of the lower diseased portion. The diseased portion was resected and excised right down to the bladder mucosa. This excision included all layers of the bladder musculature, roughly the size of the elliptical opening of the ureter. The bladder mucosa was then grasped with fine intestinal forceps and exerted and stitched with interrupted mattress

normal. The conjunctivae were slightly hyperemic and both fundi showed grade 1 to 2 irregular spasm of the arteries and terminal arterioles but no evidence of hemorrhages. The lungs were clear. Blood pressure varied from 100/108 to 111/100 and was without appreciable alteration when the patient changed from the prone to the sitting position. The heart was normal in size. There were no murmurs; the tones were of good quality, the rhythm regular and the rate 80. The liver and spleen were normal in size. Pelvic examination revealed slight tenderness in both fornices on bimanual palpation but otherwise normal. The uterus was anteverted and normal in size.

Urine.—On repeated specimens the specific gravity varied from 1.005 to 1.010 and a faint trace of albumin was present in almost all of them. There was no sugar. Microscopic examination revealed 7 to 12 pus cells, a rare red blood cell and many gram-negative bacilli and gram-positive cocci.

Blood count.—The erythrocyte count was 5,330,000 and the hemoglobin 16.5 g. or 97 per cent. The leukocytes numbered 11,000 with 59 per cent segmented, 11 per cent lymphocytes, 3 per cent monocytes and 1 per cent basophils.

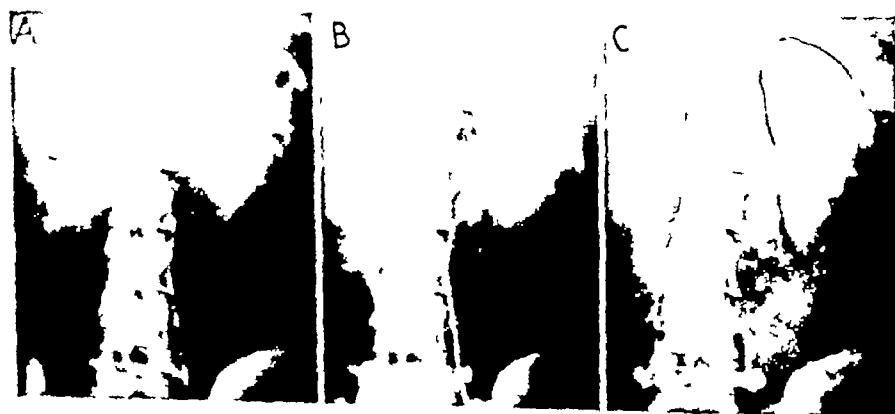


FIGURE 1

site of the anastomosis and hydronephrosis above. In all the other cases which number 12 follow-ups after a period of from 6 months to 1 year have shown that the ureteral orifice is patent, there has developed no hydronephrosis above the site of anastomosis, kidney function has improved, and the patients have been freed of the secondary infection due to the stasis present before the operation was carried out.

Out of the 38 cases operated on, irrespective of the operative procedure used, there were 11 failures. An analysis of these 11 cases discloses 10 in which the direct cause of failure was stricture at the site of anastomosis, causing a gradually

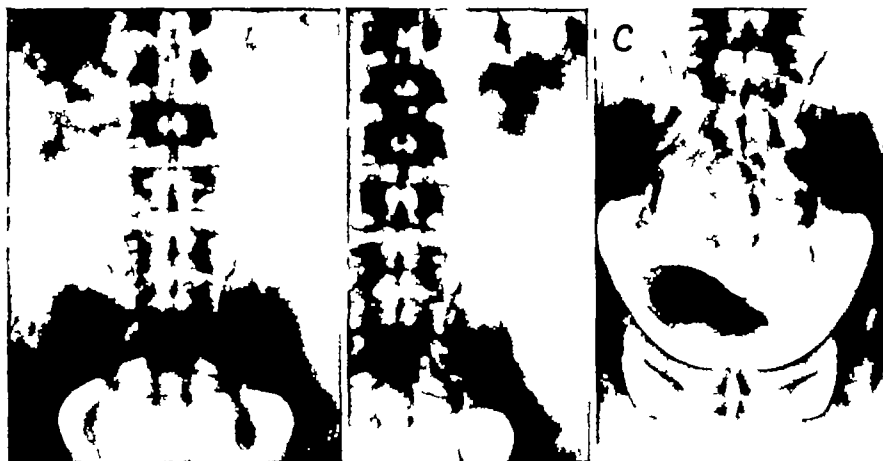


FIG. 5. A. A. K. case No. 11922. A, excretory urogram before operation. Note dilation of left ureter. B, case No. 11922. Follow-up excretory urogram after resection of 6 cm at distal end of ureter.

TABLE 2. Group 2. Anastomosis of ureter into bladder after resection of diseased portion

TECHNIQUE	NO. OF CASES OPERATED	GOOD END RESULT	FAIR END RESULT	FAILURE
Elliptical anastomosis of the end of the ureter to the bladder mucosa	13	8	4	1
Ureter implanted by making two flaps of its distal end and suturing into bladder	6	2	1	3

increasing hydronephrosis. The eleventh case developed a sinus at the site of the insertion of the T tube. Of these 10 cases, 9 had definite signs of increasing block at the ureter within two or three months of operation, and it was quite evident even then that the anastomosis was not functioning properly. The tenth case was lost sight of postoperatively, and when he returned for re-examination 3 years later, he had a huge hydronephrosis and a nonfunctioning kidney. In spite of many attempts in all these 9 cases to dilate the stricture by retrograde catheterization through a cystoscope, none of them was relieved by this method of treatment. Finally, 4 patients had to have a nephrectomy, 3 patients refused further surgical treatment, 2 cases had a re-anastomosis of the ureter after

DISCUSSION

DR THOMAS L. GIBSON (San Francisco, Calif.) Dr Sivegh deserves high praise for his excellent contribution to the surgery of the ureter. It is a field in which he has had exceptional experience. Bilharzial infestation is notoriously common in Egypt where it is endemic and exhibits a predilection for invasion of the urinary tract with the production of the most devastating lesions. He has emphasized the tendency to widespread involvement of the ureter with ultimate stricture formation and secondary destruction of the kidney from obstruction. The strictures are usually so dense and unyielding, and produce such distortion of the ureter with concomitant peri-ureteritis that they will not yield to dilatation through the cystoscope. Surgical treatment is mandatory and corrective ureteroplastic procedures tax the urologist's ingenuity and resources to the utmost.

Certain underlying principles of surgery have become well established which apply to obstructions of the ureter as well as to obstructions at the ureteropelvic junction. Two methods of treating ureteral strictures may be used: 1) the Davis-Rammstedt procedure consisting of making one or more longitudinal incisions in the wall of the ureter followed by intubation; and 2) excision of the affected segment of ureter with intubation.

Dr Sivegh has demonstrated the value of the mucosa to mucosa spatulate anastomosis of Nesbit. However, he is seemingly dubious about the value of ureteral splinting which is synonymous with intubation. I venture to say that he may have resorted to the splinting catheter or tube only in his worst cases where success was problematical at best, and that the failures he had with splinting would most certainly have turned out to be failures without splinting. An orthopedist would not think of reducing a fracture without afterwards using a splint to hold it in place. This orthopedic principle applies just as cogently to the urological problem.

Since my original paper on ureteral splinting published in the *Journal of Urology* in 1939 I have become more and more convinced of its value in all types of major obstructions in which ureteroplasty or pelvic ureteroplasty are necessary. You are all familiar with the excellent work of Davis in which he has demonstrated conclusively the ability of the ureter to bridge over large gaps and defects with the aid of ureteral intubation. It should be axiomatic that the urologist make use of ureteral splinting or intubation following operation on all intrinsic obstructions of the ureter or ureteropelvic junction associated with inflammatory and scar tissue change in or about the wall of the ureter. The period of splinting or intubation should be maintained for two weeks to two months depending upon the type and severity of the obstruction. Time does not permit entry into a discussion of the many technical details of ureteral splinting. At the present writing I find polyethylene tubing in various calibers a very satisfactory medium for splinting and intubation. It may be that polyvinyl tubing which is now being displayed in the commercial exhibits will prove even more satisfactory.

DUODENAL FISTULA FOLLOWING RIGHT NEPHRECTOMY

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Fifteen per cent of all duodenal fistulas occur after right nephrectomy. The incidence after right renal operations is reported as being 0.7 per cent.¹ Duodenal fistulas following right nephrectomy are of the lateral type (fig. 1).^{2, 3} There is a reported mortality of 40 per cent in patients with such a lesion. If duodenal operative procedures, conceived in desperation, are dangerous. But if because of a well planned therapeutic program will minimize the morbidity and mortality.

Infection and hemorrhage in the operative field, inadequate exposure, rough manipulation or instrumentation favor trauma to the duodenum with subsequent fistula formation. The fistula is recognized by the copious bile and food discharge from the wound which soon results in irritation to and digestion of the surrounding tissues. The diagnosis is confirmed by radiographic examination.

PATHOLOGIC PHYSIOLOGY

Normally the proximal gastrointestinal tract elaborates large quantities of fluid and electrolytes, most of which are subsequently reabsorbed (table 1). Up to 5 liters may be lost through a duodenal fistula in 24 hours.⁴ The fluid contains approximately 100 mEq of chloride and 20 mEq of potassium per liter.

The patient soon develops hypochloremia, hypopotassemia and alkalosis. If the untreated dehydration is soon apparent. The kidney is unable to excrete the nitrogenous waste products and uremia ensues.

Figure 2 depicts the composition of the plasma in the normal and in a patient with a duodenal fistula. There is a decrease in chlorides and a compensatory increase in bicarbonate. There is an increase in the organic acid, sulfate and phosphatements. There is a relative increase in the protein fraction which is the result of the dehydration.

MANAGEMENT

GRANULOMA OF THE URETER

IRVING HILBLER

Intrinsic obstructions of the ureter, unless caused by stones, strictures or the like, are due to tumors. The majority of ureteral tumors are malignant, benign tumors are rare, and since benign tumors are mostly papillomas, one cannot be sure of their benign character. A few benign inflammatory obstructive lesions have been reported by W. F. Braasch and N. V. Hurley, Patch, and Hamer, Mertz and Wishard. To this small number another case shall be added.

CASE REPORT

Mr. G. B., aged 70, a housewife, was first seen in 1945. She gave a history of having had 6 children and having been weak and nervous almost all of her life. She complained then of pain in the right upper quadrant of the abdomen, frequency and dysuria. The diagnosis was cholecystitis, carunculi urethricae and cystitis. The kidneys and ureters were normal. The caruncle was fulgurated, the cystitis and cholecystitis treated conservatively. On dismissal in 1945 the patient was without complaints. She was not seen again until December 1948. This time she complained of frequency of 7 months' duration, loss of appetite, loss of weight and possibly low grade fever (Her temperature was not taken). She underwent treatment elsewhere but did not improve. On examination in my office on December 31, 1948, urine showed 1 plus albumin, many pus cells, no hematuria. Cystoscopy revealed normal bladder and normal ureteral orifice. It was evident that the pus in the urine was coming from the upper urinary tract. I advised complete urological study but it was about 4 weeks before I saw the patient again, suffering from colicky pain in the right kidney region. Demerol relieved the pain but the colic recurred the next day. I insisted on immediate hospitalization for complete urological investigation.

On admission to St. Joseph's Infirmary, the urine showed 1 plus albumin, specific gravity 1.016, some casts and pus cells 10 to 15 per high power field, hemoglobin 80 per cent, red blood cells 3,803,000, white blood cells 13,650, Kahn negative, blood chemistry normal. The blood pressure was 160/80.

Cystoscopy and pyelography were done under local anesthesia. A ureteral catheter was passed easily up to the left kidney pelvis. On the right side the ureteral catheter met an obstruction 3 cm. above the bladder. Urine from the right kidney was loaded with pus; urine from the left kidney was normal. Culture of urine from the left kidney showed no growth; culture of urine from the bladder and right kidney showed colon bacilli. Indigo carmine injected intravenously appeared in 3 minutes from the left kidney and no elimination of dye from the right kidney was observed.

Pyelography demonstrated a normal left ureter and left kidney and a 2 cm. long filling defect starting 3 cm. above the bladder and a dilated tortuous right

Presented at annual Meeting, Southeastern Section, American Urological Association, Boca Raton, Fla., March 21, 1949.

the lower third of the ureter and finally the ureter, including its intramural part in the bladder, severed. The impression gained by palpation was the same as one has by feeling a soft ureteral papilloma. The ureteral wall was smooth, and showed no sign of peri-ureteritis or excessive adhesions. The operation lasted not much more than an hour and the patient left the operating room in good condition. Convalescence was uneventful. The patient was dismissed from the hospital with normal urine and physically in good shape.

Photographs of the specimen consisting of the right kidney and ureter were taken (fig. 2).

On inspection of the opened ureter the tumor gave the impression of a very well circumscribed, yellowish looking lipoma of the ureteral wall occluding the ureteral lumen.

Pathologic report. The kidney was of average size and shape externally. The capsule stripped with ease. The outside of the kidney was smooth for the most part and with a very slight granulation of its cortical surface. An incision made into the kidney, exposing the pelvis, showed that the pelvis was somewhat dilated, being perhaps three or four times as large as normal with an estimated capacity of about 40 cc. The pelvic epithelium was smooth, although congested; no definite ulceration was seen in the pelvis. In the upper pole of the kidney there were some peculiar lesions. First of all, there was a cyst in the very uppermost part about 8 mm. in diameter. This lay well within the renal parenchyma. It had a smooth lining and contained dark, clear fluid. In the pyramid, next to the uppermost pyramid, there was a peculiar abscess. This had replaced practically all of the medulla of this particular pyramid, and had extended out into the cortex so that normal renal structure was destroyed. This lesion was 1.6 cm. in diameter. The center was necrotic and was filled with yellowish thick matter resembling pus. There was a wavy reddish-brown line around the abscess, which looked like a line of granulation tissue demarcating the center from the fixed tissue on the outside. As indicated, the tip of the pyramid involved was not ulcerated. The tissue around the abscess had a pale grayish-white color.

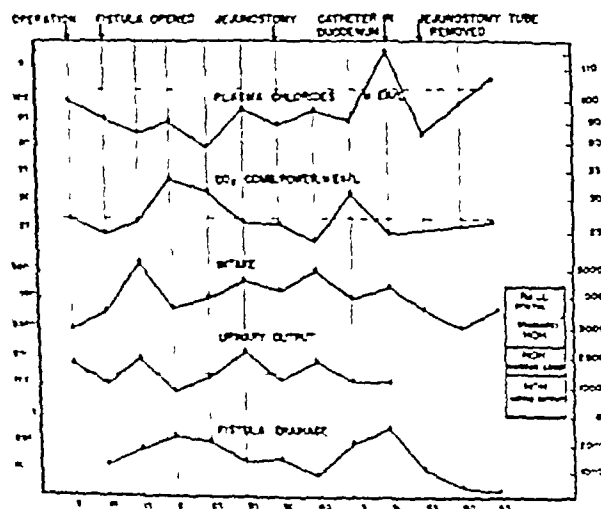
The ureter was thicker and larger than usual, with a diameter about three times normal. It was congested, and the wall was somewhat less resilient than usual. The epithelium appeared to be intact. The lower end of the resected specimen presented a peculiar nodule in it. This was just about 3 cm. above the place where the ureter was divided. The nodule was 1.1 cm. long from above down, and 8 to 9 mm. in diameter from side to side. It lay in the wall of the ureter, occluding the lumen almost completely, but did not communicate with the lumen. The lumen passed over one side of this nodule. No ulceration was present. The nodule felt fairly firm. A slice made through the center of it showed that the center was yellowish and apparently necrotic and perhaps purulent. Around the edge there was a capsule or outer wall of pale yellowish white tissue that looked like fibrous tissue.

Microscopic sections. Representative sections were made from the peculiar abscess lesion in the kidney described above. This was in reality a cystic area partly lined with epithelium somewhat like that of the tubules in the kidney.

re-obliteration of the duodenum. This was closed in 3 layers. On the third postoperative day a watery bile stained drainage from the wound was noted. It was soon evident that a duodenal fistula was present (fig. 3).



Fig. 2. Upper gastrointestinal study of patient with duodenal fistula. A thin column of contrast medium entering fistula. Mercury bag of Miller-Abbott tube lies in the fistula.



power revealed a round wall which was substituted by and covered practically completely by granulation tissue, the consistency of which shall be discussed later.

The wall showed a loosely arranged connective tissue, partly containing smooth muscle fibers. It contained also a few blood vessels and showed an adventitia-like tissue consisting mainly of fatty tissue. The elastic fibers of the supplying blood vessels were very well preserved but only fragments of this structure were noted within the wall. The coat mentioned previously and described grossly showed islands of cells which were round or ovoid in shape, offered an eccentrically or centrally located nucleus, balloon in form and loaded, most probably, with lipoids, as proved by the evidence of numerous fine vacuoles. Most of the cellular elements, however, were either lymphocytes, plasma cells, large mononuclears and surprisingly numerous eosinophilic leukocytes. In one instance a plug was attached to the coat consisting practically solely of pus cells. The coat contained a delicate framework of fibrils and connective tissue, and had a tendency to infiltrate the wall, also within the infiltrating elements the presence of a large amount of eosinophilic leukocytes was somewhat surprising. Be that as it may, there was no evidence of malignancy and one was most probably dealing with a circulating chronic inflammatory process of the ureter, also referred to as granulomatosis. **Diagnosis:** Granulation tissue tumor of the ureter, inflammatory in nature.

Since only colon bacilli were cultured in the urine, it was fair to assume that they were the offending organism. It is known that colon bacilli may cause destruction resembling tuberculosis in the urinary tract.

Reviewing the literature, I did not find an inflammatory tumor-like lesion of the same microscopic appearance. None of the described lesions was so well localized as the one described above. It resembles a tumor more than an inflammatory lesion and particularly so because the tissue surrounding the lesion did not reveal signs of inflammation on inspection. The majority of the reported granulomas were discovered accidentally, secondary to other pathological conditions in the kidney, bladder and ureter.

Brusch and Hurley reported 'a granuloma of the ureter' in a case of chronic inflammation around the left ureteral meatus and patchy filling defects in the lower half of the corresponding ureter. Microscopic examination showed tissue of inflammatory character and localized hemorrhagic edema of the lower 13 cm. of the left ureter. They reported also papillomas of inflammatory character in the bladder and granulomatous tissue around a foreign body or following surgery and finally a case of syphilitic granuloma of the bladder.

Le S. Patch reported a case in a 10-year-old boy with nephrolithiasis, hydronephrosis with a pea-sized mass in the ureter 5 cm. below the ureteropelvic junction. This was described by the pathologists as a grayish white granular irregularly outlined area bordered by a narrow zone of the mucous membrane consisting microscopically of lymphocytes, plasma cells and occasional eosinophils between fibroblasts and thin walled dilated capillaries. H. G. Hamer described as ureteral granuloma a purplish gray easily bleeding granular area in the ureter

countered in tumors was also encountered in a few reported cases of granuloma but not in this case.

As to therapy, I do not think anything short of removal of the kidney and ureter would have been indicated in the reported case. It would have been impossible by the use of antibiotics to influence the obstructive granulation tissue in the ureter. It is also questionable whether the abscess in the kidney would have responded to antibiotic treatment without establishment of proper drainage of the cavity.

SUMMARY

A case of granulation tissue tumor of the ureter was described which gave all the characteristic findings of an obstructive ureteral tumor. Treatment by nephro-ureterectomy was successful, and the 70 year old patient is in perfect shape more than a year after the operation.

I wish to express my appreciation to the pathologists, Dr. Everett Bishop, Dr. B. Matthews, and Dr. P. R. Rezek for their most helpful cooperation.

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operated on again for excision of stricture due to the development of hydro-nephrosis. 1 patient had to undergo nephrectomy, and in 1 case the result was fair.

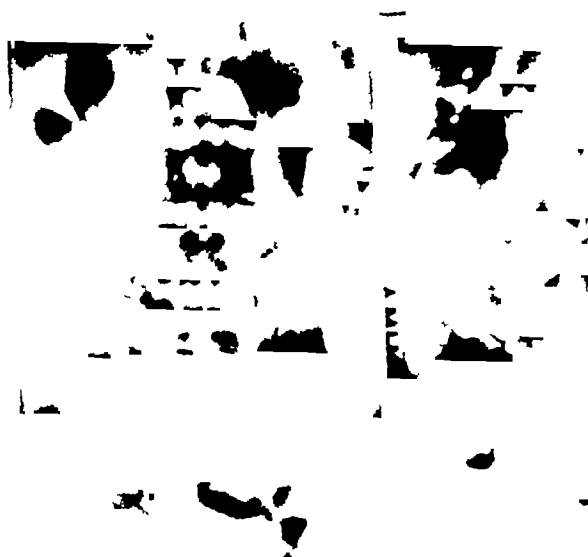


Fig. 1. *A*, Case No. 3700. *A*, Elliptical end to end anastomosis after resection of 5 cm. third of right ureter. No splinting catheter used. *B*, Case No. 39500. Retrograde dilatation of right ureter after 1 year.



Laboratory reports before surgery disclosed 4.3 million red blood cells per cu mm of blood, 11.7 gm hemoglobin per 100 cc of blood, 6,900 white blood cells per cu mm of blood, with 5 per cent eosinophils, 64 per cent neutrophils and 31 per cent lymphocytes; nonprotein nitrogen 22 mg per cent. Catheterized specimen of urine: specific gravity of 1.027, amber, cloudy, acid, albumin 100 mg per 100 cc, many pus cells, and 3 red blood cells per high powered field.

The second cystoscopic examination the day prior to surgery revealed the bladder mucosa moderately congested, right ureteral orifice reddened, ulcerated and edematous, with an inability to pass the ureteral catheter beyond 1 cm.

With a preoperative diagnosis of a mass in the right ureteral stump, the patient was scheduled for surgery. Through a right Gibson incision, a large mass 12 by 7 by 4 cm, adherent to bladder, peritoneum and renal fossa was exposed and



FIG. 1

resected. The patient had a satisfactory postoperative course except for a left saphenous thrombosis successfully treated with anticoagulant therapy. The patient was discharged on her eighteenth postoperative day in apparently good condition.

The specimen consisted of an indurated in places at its periphery friable mass 3 by 2 cm which was attached in a linear direction to a mass of semifirm tissue 12 by 7 by 4 cm. Microscopic examination (fig. 2) revealed the indurated and friable tissue consisted of edematous ureter and adventitious tissue. The normal mucosa is replaced by anaplastic epithelial cells which form papillae and also infiltrate the subepithelial connective tissue, circular muscle bundles to the level of the longitudinal muscle bundles. The anaplastic epithelial cells have a varied morphology and resemble transitional cells, squamous cells, and spindle cells. The wall of the ureter is edematous and also infiltrated with plasma cells.

reason being that renal pelvic neoplasms metastasize frequently by direct extension or drop metastasis to the ureter and even to the bladder mucosa.

Carcinoma of the renal pelvis and ureter may take origin from another source as this case illustrates. When metastatic carcinoma of the ureter follows a case of malignancy in the pelvis or kidney parenchyma, the pathology and etiology can be demonstrated (Baley, Fort and Harlin, Howarth Mombierets). However when a kidney is removed for reasons other than a tumor, such as an infection or calculi and many years later the ureteral stump that remains becomes the seat of a malignancy, an entirely different process is demonstrated.

According to Herbut the direct cause of carcinoma of the ureter is unknown but the most common theories are leukoplakia, epithelial inclusions, mechanical or inflammatory irritation, carcinomatous rest, and excretions of carcinogens in the urine. Therefore this is an example of origin by metaplasia or leukoplakia. Boyd remarks that leukoplakia is a rare accompaniment of chronic inflammation. The mucosa in these cases is an epidermoid change, a metaplasia of the transitional type of epithelium to a squamous stratified type. This may be regarded as a precursor of the nonpapillary type of carcinoma. In this case the squamous cell metaplasia produced by the infection later developed into squamous cell carcinoma. McCrea showed how the repeated insults to the tissues over extended periods by exacerbations, followed by low grade, continued infection most probably induce this type of metaplasia.

COMMENT

The case presented illustrates some of the known facts of carcinoma of the ureter. The etiology was evidently chronic infection and irritation. Fifteen years ago the patient had a right ureteral calculus infected hydronephrosis and, after nephrectomy, developed pyo-ureter. The pyo-ureter was so extensive that three hospitalizations were required in the year following her nephrectomy. The pyo-ureter was never completely controlled but the patient developed a tolerance and immunity to her infection and remained relatively asymptomatic subjectively. Periodically the patient did experience episodes of abdominal pain, backache and urinary distress. The inflammatory process and possibly the malignant changes became evident 6 months prior to the time she sought medical treatment again. When she presented herself for further study, the findings were presumed to be those of an infected ureteral stump. Gross and microscopic examination of the excised mass revealed infected necrotic tissue and squamous cell carcinomatous degeneration in one area produced by a squamous cell metaplastic process of the chronically infected tissue.

We have learned from this case and the review of the literature that total ureterectomy should be done as the procedure of choice in treatment of chronically infected kidneys, tumors of the renal pelvis, polyposis and pyo-ureter where surgical treatment is indicated. Only by this radical procedure can chronic pyo-ureter and possibly carcinoma of the ureteral stump be eliminated. However because of the rarity of carcinoma of the ureter in uncomplicated cases, one should remove only that portion of the ureter reached without additional trauma or incision.

NEW SIGMO-URETEROSTOMOSCOPE FOR TREATMENT OF IMPLANTED URETER

A. H. KLEIMAN

Several months ago, I saw a patient with ureteral strictures that had resulted from ureterosigmoidal anastomosis. Pyelography showed a pronounced bilateral hydronephrosis and pyelonephritis. The patient's refusal to undergo additional major surgery posed the problem of finding some other means of therapy. It occurred to me that an instrumental approach might solve the difficulty, and I, therefore, combined a modified sigmoidoscope with a special telescopic unit. The construction of the instrument was discussed with Mr. Frederick J. Wallace of the American Cystoscope Makers, Inc. and with his expert technical aid and suggestions a practical "sigmo-ureterostomoscope" was finally evolved.

The new instrument furnishes excellent forward vision by employing a telescopic unit of brilliant and precise illumination. It presents the urologist an opportunity not only to treat pathology of implants, but to observe physiologic changes resulting from a shunting of the urine to the sigmoid. Successful passage of this instrument is not difficult. It becomes simple with experience gained by an adequate knowledge of anatomy, and gentle, sympathetic instrumentation. The technique will be explained in detail later in this article. The liberal use of chemotherapy and antibiotics makes the procedure safe and practical.

Before performing major renal surgery for the complications of the strictures of ureteral implants an investigation with the sigmo-ureterostomoscope is recommended.

The new instrument (fig. 1) includes a sheath, obturator, special telescope unit, eye piece and light carrier.

The sheath has been made in two sizes. The shorter tube is 11 inches in length and 0.7 inches in diameter. The longer tube, which is 13 inches in length and $\frac{1}{2}$ of an inch in diameter, is especially designed for manipulation of the higher implanted left ureter. The proximal end of the sheath has a large, round flange. This presents at its roof a small slit (A-1) which accommodates the fastening pin of either the obturator, eye piece or telescopic unit. When the pin is made secure by a large fastening screw (A-2), the sheath becomes air and water tight.

An auxiliary tube (A-3) enters the flange at an angle to join the sheath. The auxiliary tube houses the light carrier and serves as an outlet for irrigating medium and debris. A metal plug seals the auxiliary tube when it is not in use. Petcocks (A-4) are located on both sides of the flange; these serve as an outlet for either water or air.

Light for the sheath proper is furnished by a standard ACMI light carrier. This includes a large electric bulb, enclosed within a plano-convex lens and a thin metal cartridge. It fits snugly into the auxiliary tube and directs a beam of light to the distal end of the sheath. The light carrier is employed during passage of the sheath to the sigmoid. The standard ACMI battery and conducting cord

1. Read before the Gynecologic and Urologic Section of the New York Academy of Medicine, December 20, 1951.

proximal portion of the telescopic frame, and terminate just proximal to the deflector. They have a diameter of number SF, and run along the floor of the working unit. Sealed off from the lumen within the sheath, they are designed to minimize infection during passage of the catheters.

An excretory urogram is made before instrumentation in order to guide the operator as to approximate site of implant. It also serves as an index of renal function and may help reveal dangerous complications. In cases where serious ulceration, abscess, peritonitis or ureteral slough are suspected, sigmoid uretero-tomography is contraindicated.

TECHNIQUE

In the selected case, the patient is prepared with a low residue diet for 72 hours prior to instrumentation. A gram of sulfasuxidine and 250 mg. of aureomycin q.i.d. are administered at the same time. A purge is used the evening before instrumentation. To avoid bowel spasm, traneptin and phenobarbital (140 mg. t.i.d.) are prescribed 24 hours prior to instrumentation. Morphine sulphate and atropine injected shortly before the procedure is also helpful in this connection. A 20 cc. rectal instillation of 2 per cent novocaine in a water soluble jelly is useful for undue spasm, if introduced 15 minutes before the examination. When retrograde studies are contemplated the procedure should be performed in a hospital for obvious reasons.

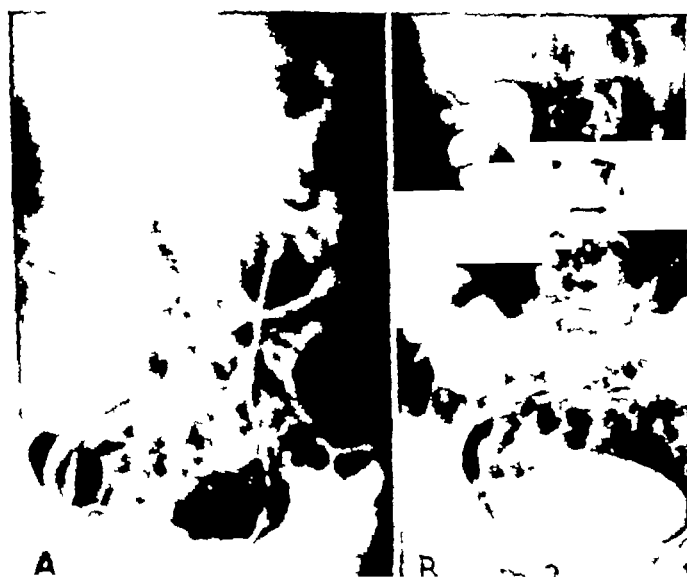
Patients who have undergone implantation appear to have undue spasm of the colon and rectum during instrumentation. This frequently results from apprehension but may be due to an inflammatory reaction of the bowel from the urine and infectious material leaving the kidney. By using antispasmodic agents, gaining the confidence of the patient, and exercising gentleness in technique, the procedure is simplified.

In order to facilitate passage of the instrument, it is necessary to place the patient in the proper position. The inverted position is ideal because it reduces the degree of sigmoidal flexion. The position is best attained with a special sigmoidoscopy table. By directing the head downward towards the floor, supporting the weight on the flexed elbows, and avoiding pressure up on the pelvic and abdominal wall, passage of the instrument is simplified. Where a special table is not available the cystoscopic table with an adjustable stool and pillow may be substituted (fig. 2). The patient first lies on his abdomen and is gradually guided downward and forward to the supporting stool. The patient's weight is supported by the abducted thighs above and the hands and anterior chest wall below.

A preliminary digital examination is made prior to instrumentation. This is a useful guide for the passage of the instrument and reveals spasm or rectal disease. For convenience of description the passage of the instrument is divided into three phases. In the first phase the warm lubricated sheath, with obturator locked in place, is passed to the sigmoid in the conventional manner. When it is introduced in a forward direction into the mass the distal end of the instrument is directed towards the umbilicus (fig. 2). During its passage through the

the filling defect (fig. 1 A). The right kidney pelvis and calyces were amply filled, but definitely dilated. On pyelography repeated 2 1/2 hours under general anesthesia the right ureteral catheter was passed 0.5 cm higher into the ureter but the ureteropyelogram was essentially the same. The excretory urogram was suggestive of hydronephrosis: a dilated ureter and calyces in the upper pole of the kidney indicating abscess formation (fig. 1 B). The examination of the left kidney was essentially normal.

Postoperative findings: the diagnosis of tumor of the lower third of the right ureter, ureteritis, hydronephrosis, and abscess in the right kidney was made. The regular outline of the filling defect, the lack of bleeding on touch with the ureteral catheter on several occasions, and the impossibility of palpating the mass by pelvic examination made the diagnosis of benign tumor very probable.



sigmoidal junction (fig. 3, B). The prominent rugae and its anterior and somewhat to the right position identify the site. The location of the junction varies with the degree of intussusception and immobilization, at the time of implant. It is normally in the region of the third sacral vertebra.

In the third phase, the instrument is passed forward under vision, directing the lens piece first to the left in a backward direction, then, gently in the opposite direction. When the sheath is passed as far as possible into the colon, irrigation and suction are applied. A standard alligator cotton carrier is employed to wipe the mucosa. The sigmoid is washed clean with several washings of the diluted zephiran solution, and the light carrier is removed, and the telescopic unit is introduced. With the working element locked securely, the ureteral orifices are sought. Exploration is facilitated by careful distention with solution or air. The implants are most easily discovered by slow withdrawal and rotation of the instrument from side to side. Because of the patient's inverted position the orifices will be found nearer to the floor of the mucosa rather than the roof. In cases of difficulty, intravenous injection of indigo carmine may be used for the identification of these openings, once recognized, their exact distance from the anus is recorded for future reference. When passed through the telescopic unit, the ureteral catheters are irrigated with zephiran solution, prior to passage up the orifice. Manipulations within the ureter are made with care to avoid undue force or pressure.

If a retrograde pyelogram is desired, a special elongated ureteral catheter is passed up the orifice to the renal pelvis. The catheter is held secure as the instrument is withdrawn. Patient is replaced in position for x-ray studies. A pyelogram is then made in the usual manner. Post-instrumental care includes hydrotherapy, chemotherapy and antibiotics. Antispasmodics are used when indicated. The afebrile patient leaves the hospital the morning after the examination.

Acknowledgement is made to the Institute of Vascular Medicine and the Urology Service of Cornell Medical Center for their generous offer of clinical facilities and material.

SUMMARY

The sigmoid ureterostomoscope is presented as an aid in diagnosis and treatment of pathological conditions resulting from ureterosigmoidostomy.

The instrument consists of sheath, obturator, eye piece, and a working telescopic unit. An irrigating medium is employed to facilitate sigmoidal vision and instrumentation of the implanted ureteral orifice.

Success of procedure depends on skilled passage of the sheath to the site of implant and careful ureteral manipulation.

The new instrument is designed to assist in the elimination of laparotomy, nephrostomy, nephrectomy or reimplantation in the treatment of stricture complicating uretero-intestinal surgery.

with the possibility of the electrolyte disturbance developing in a manner analogous to the reabsorption of an acidifying chloride salt was clearly presented by these authors. We have not observed these changes to occur in ureterosigmoidostomies or in patients with only one kidney which drains by nephrostomy. Lewis and Odell demonstrated normal excretory capacity for chloride in a patient subjected to nephrostomy 9 years after uretero-sigmoidostomy. This patient had severe hyperchloremic acidosis prior to nephrostomy drainage. It also has been our experience that lavage of the colon and an indwelling rectal tube (especially at night) are measures of decided benefit in limiting reabsorption of urine and in correcting both the acidosis and elevation of blood urea. The promptness of therapeutic response to procedures which limit chloride intake and provide adequate sodium intake is further evidence that these changes are on the basis of chloride absorption rather than failure of renal excretion.

A syndrome quite similar to that seen in patients can be produced in the experimental animal by anastomosis of the dome of the bladder to the sigmoid colon. Urinary obstruction is largely eliminated in this procedure since the terminal ureters are not disturbed, thus retaining their normal ureteral orifices and preventing the disturbances in function that follow either peri-ureteral cicatrization or ureteral reflux. Furthermore, the electrolyte imbalance in these animals can be promptly corrected by cutaneous sigmoidostomy proximal to the point of vesicosigmoidostomy. This is presumably accomplished by limiting the flow of urine to the distal portion of the colon just above the rectum where little or no absorption occurs.⁶

It is possible to distinguish the electrolyte changes that occur on the basis of absorption from those that occur on the basis of impaired renal function as occurs following obstruction. The colon is impermeable to the sulfate ion^{7,8} and only slightly, if at all, permeable to the phosphate ion. Impaired renal function from obstruction results in retention of both sulfates and phosphates¹⁰ with an increase above the normal serum level of 2.5 to 5 mg. per 100 cc. for sulfate and 3.7 to 5 mg. per 100 cc. for phosphate. These changes may occur before other tests reveal any change in kidney function.¹⁰⁻¹¹

In the presence of normal kidneys depression of plasma HCO_3^- following uretero-sigmoidostomy is probably due to reabsorption of acid radicals accompanied by cations other than those which make up the fixed base (Na, K, Ca, Mg) of the body. The increase in blood chlorides indicates that chlorides are at least one of the reabsorbable anions. The most logical cation to accompany chloride is ammonium.¹² It is known to be rapidly absorbed from the upper gastrointestinal tract¹³ and is universally increased in the colon following uretero-

⁶ Boyce, W. H. *J. Urol.* **65**: 241, 1951.

⁷ Goldschmidt, S., and Davison, A. B. *Am. J. Physiol.* **48**: 440, 1919.

⁸ Goldschmidt, S., and Davison, A. B. *Am. J. Physiol.* **48**: 450, 1919.

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¹⁰ Durr, W., and Holman, S. *J. Biol. Chem.* **55**: 183, 1923.

¹¹ Kohn, J. A. *Clinical Diagnosis by Laboratory Examinations*. New York: Appleton Century Crofts, Inc., 1950, 2nd ed., p. 135.

¹² Barst, M. M., Douglas, C., Haldane, E. S. B., and Priestley, J. G. *J. Physiol.* **57**: 41, 1922.

This second method had two distinct disadvantages. The first was the possibility of dilution of the ammonium chloride solution by material from the duodenum. This objection is largely theoretical, since the solution obtained from the colon

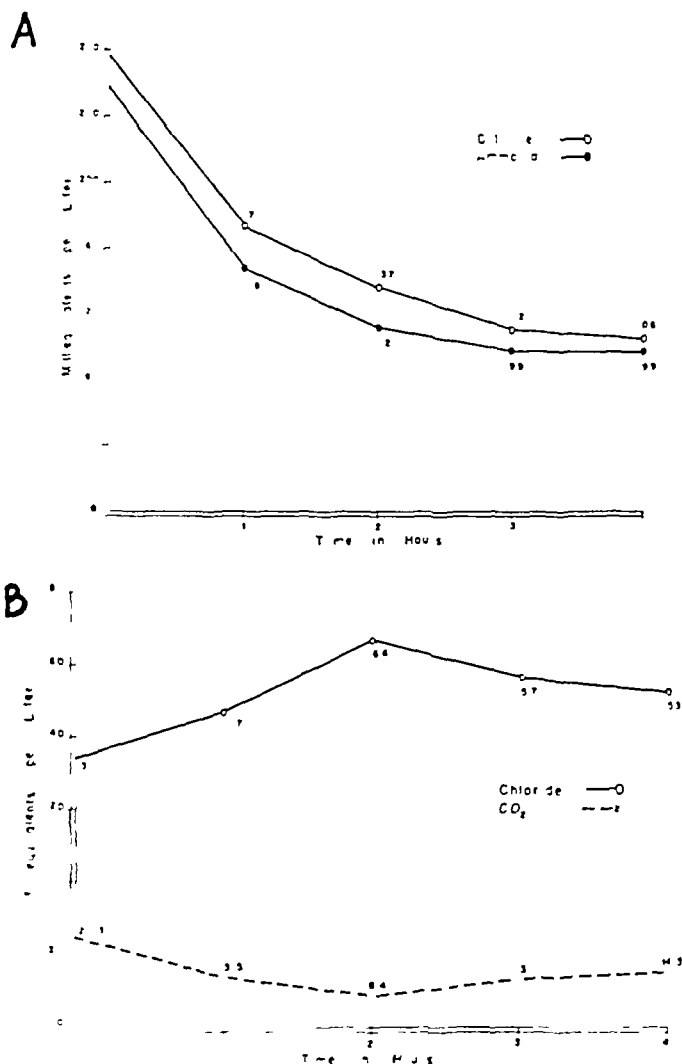


FIG. 1. Dog No. 305. A, concentration of ammonium nitrogen and chloride remaining in ammonium chloride solution containing 257 milliequivalents of ammonia nitrogen per liter after instillation into colon. Both NH_4^+ and Cl^- ions were actively absorbed. B, whole blood chloride and plasma CO_2 combining power after instillation into colon of ammonium chloride solution containing 257 milliequivalents of ammonia nitrogen per liter. The CO_2 determinations were made simultaneously at same time intervals in experiment shown in A and show increase in whole blood chlorides (with depression of HCO_3^-) as chloride disappears from solution in colon.

at the end of the experiment was always little more than half of the quantity injected due to absorption. The additional difficulty was in obtaining samples. After 2 hours the solution had migrated to the rectum and samples could not be

urea was therefore an indication of increase in either blood urea or ammonia or both.

There was an average loss of fluid from the bowel of 40 per cent with a corresponding increase in the total nitrogen and chloride absorbed. Since the absorption of water cannot be measured until the end of the experiment it cannot be accurately proportioned as to the time interval.

The concentration of ammonia nitrogen of 300 mg. per 100 cc. in the solution is not greater than that which may occur in the human following ureteroigmoideostomy. Normal human urine contains an average of 600 mg. of ammonia nitrogen per 24 hours and this may increase to 1200 mg. under certain conditions. This does not take into consideration the 11,653 mg. of ammonia nitrogen that may arise from the bacterial decomposition of 25 gm. of urea excreted each 24 hours.

DISCUSSION

Ammonium and chloride ions are absorbed from the colon of the dog in proportions approaching their molecular ratio. The highly reactive ammonia portion of the ammonium chloride molecule immediately becomes a part of the total nitrogen in the metabolic pool. The disposal of excess blood ammonia by conversion to urea is a function of the liver and the production of ammonia by the kidney a mechanism for conservation of base, two processes of nitrogen metabolism entirely separate and independent. The chloride ion is then free to act as an equivalent of hydrochloric acid requiring neutralization by fixed base of the plasma alkali reserve (largely sodium bicarbonate). There is an adjustment of the plasma anions with an equivalent respiratory release of carbon dioxide reflected in a reduction of plasma HCO_3^- . Another immediate effect of the absorption of chloride is excretion by the kidney of some of the excess chloride in combination with fixed base (largely sodium chloride). There is conservation of fixed base by ammonia formation in the kidney which is instigated by the fall in plasma bicarbonate. This defensive mechanism does not reach a maximum for several days following invasion of the plasma by a strong acid. This form of acidosis is actually a recapitulation of acidosis following the simple ingestion of ammonium chloride by individuals with normal kidneys.

Increased ammonia formation by the kidney which deposits urine into the colon may increase the acidosis by increasing the quantity of ammonium chloride available for reabsorption thus establishing a round-robin of ammonia and chloride exchange between the colon, plasma, and kidney (fig. 3). The intra-colonic conversion of urea to ammonia contributes an additional supply of the cation.

The patient in such a state requires base bicarbonate to furnish an equivalent of fixed base (sodium) to cover the reabsorbed acid radicals (chloride and possibly organic acids) excreted into the colon and to aid the kidney by a reduction in the necessity for ammonia formation. This ultimately reduces ammonia excretion and its availability as the necessary cation for ammonium chloride reabsorption. Infusions of sodium chloride can only aggravate the condition.

of forming a gel in the colon which will retain urine and delay absorption has a sound basis in theory. Agar-agar is an ideal material. This procedure has the major disadvantage of adding bulk to the diet of a patient who often has anorexia to a degree that prevents an adequate caloric intake. Furthermore, the diffusion coefficient of ammonium chloride and urea is high and even approaches that of hydrogen and oxygen so that the impedance to their diffusion in gels is actually small.²⁴

We have found the following regimen to be helpful in our cases in controlling this unusual acidosis that may follow ureterosigmoidostomy.

1) Careful attention to emptying the rectum by tube in the immediate post-operative state and by urging the patient not to engage in retention marathons.

2) Alkaline ash diet which not only furnishes base in a palatable form but reduces the excretion of urea and ammonia.

3) Protein intake not in excess of body requirements to reduce urea excretion and the possibility of its conversion within the bowel to ammonia. Excess protein intake also augments intracolonic ammonia formation.

4) Low-salt (chloride) intake. In the hospital this may be accurately restricted to 2 to 4 gm. sodium chloride per 24 hours, and the sodium deficit made up in other ways (citrate, lactate, or bicarbonate). In the out-patient clinic the patient is instructed not to add salt at the table or to indulge in salty foods but to continue to use the usual quantity of salt in cooking. This will provide about one-half the daily requirement of sodium. The patient who does not respond to this may prepare meals separately from the remainder of the family and add a measured quantity of salt.

5) Oral fluid intake of at least 2,000 cc. water evenly spaced throughout the day and in addition to food and liquid taken with meals.

6) Sodium citrate 10 per cent solution in doses of 4 to 20 cc. 3 to 4 times daily which provides a palatable form of alkali administration, the citrate is far superior to the bicarbonate for this purpose. The mild salty taste is easily masked by fruit juice or fruit syrups. Sodium citrate is readily absorbed but the sodium ion slowly becomes available to the alkali reserve as the citrate is metabolized. This prevents the sudden wide variations in available sodium that occur with the administration of sodium bicarbonate. The many complications that may follow ingestion of sodium bicarbonate—gastric distress,²⁵ sodium retention and edema with cardiac and renal impairment—are well recognized.²⁶⁻²⁸ We believe such complications are much less likely to occur with sodium citrate than with sodium bicarbonate. Not only is the citrate more slowly absorbed and utilized but the patient is reluctant to increase voluntarily the dosage of an unknown prescription where as there is a tendency to regard 'soda' as innocuous and so voluntarily to increase the dose to dangerous levels.

¹ Friedman I. J. Am. Chem. Soc. **52**: 1311, 1930.

² Burkett D. G. J. A. M. A. **139**: 27, 1949.

³ Army Medical Research Unit, Oxford. Effect of large doses of alkali on kidney function. Lancet **2**: 701, 1945.

⁴ Burkett C. H., Burrow B. S. and Commons R. R. J. Clin. Investigation **29**: 104, 1951.

⁵ Hardt E. L. and Laver A. B. Arch. Int. Med. **31**: 171, 1923.

streptomycin, penicillin, or terramycin 3) When an alkaline ash diet was administered. It is evident that the efficacy of the alkaline ash diet lies in the provision of basic ions all of which will displace ammonia from the chloride in accordance with their position in the periodic table ($\text{Ca} > \text{Mg} > \text{K} > \text{Na} > \text{NH}_4$). In this manner less absorbable chloride salts are substituted for the more absorbable ammonium chloride.

It should be emphasized that the appearance of a normal blood urea in combination with a low plasma carbon dioxide combining power and elevated serum chloride concentration is no indication that ammonia was not reabsorbed with the chloride ion. Immediately after absorption ammonia becomes a part of the metabolic pool of nitrogen and variations in the level of blood urea are, in the presence of normal renal function, a reflection of nitrogen metabolism and not of acid-base imbalance. Although urea may diffuse into the blood from the recto-sigmoid, this in all probability constitutes only a small additional load which the normal kidney promptly excretes. (Urea load in the normal person may vary with the diet from 4 to 50 gm. per 24 hours without elevation of blood urea to abnormal levels.)

It is evident that the acidotic state may develop in an individual from either retention of acid radicals or loss of base, or a relative combination of these changes. The state is not necessarily a reflection of renal insufficiency although any form of renal insufficiency and especially tubular damage and back pressure will accentuate any acidosis. The etiologic factors producing acidosis may therefore be multiple. Renal insufficiency when present may be of such degree that the acidosis is refractory to correction by alkali administration.

It is concluded in view of the experimental work presented and in view of observations on the two additional cases that impairment of renal function will surely accentuate the acidosis of absorption but that it is not entirely essential to the development of the acidosis which follows diversion of urine to the colon by various techniques. An important determining factor would also seem to be the electrolyte composition and concentration (especially ammonia and chloride) of the intracolonic contents.

CASE REPORT

A 63 year old white man was admitted to a neighboring hospital on April 29, 1949 because of intermittent, painless, gross hematuria of 5 years' duration. At cystoscopy a large papillary tumor involving the base of the bladder and trigone was seen. Biopsy showed a grade 1 papillary carcinoma. Excretory urograms revealed moderate right hydronephrosis. Renal functions were normal. On May 10, 1949 a bilateral ureterosigmoidostomy was performed according to the Coffey technique. An uneventful postoperative course ensued, and on May 31, 1949 a total cystectomy, prostatectomy, and bilateral seminal vesiculectomy was performed. A local grade 1 papillary carcinoma of the bladder 5 cm in diameter was found. Prompt recovery from the operation followed. At the time of discharge from that hospital on June 20, 1949 the nonprotein nitrogen was normal and excretory urograms revealed moderate dilatation of the ureters and pelves bilaterally, more pronounced on the right. The patient's general condition was good. One week later he first noticed incontinence of urine and feces. Because of this complication he was admitted to this hospital on July 18, 1949. Physical examination revealed a temperature of 101°F, tenderness in the right flank and a large edematous, inflamed, thrombosed hemorrhoid. There was complete loss of anal sphincter tone with continuous dribbling incontinence of urine and feces. There was also a suprapubic incisional hernia approximately 6 cm in diameter. Excretory urograms showed moderate bilateral hydronephrosis and hydro-ureter. The nonprotein nitrogen was 25 mg per cent. Blood counts were normal.

The thrombosed hemorrhoid was incised and evacuated. The right flank tenderness disappeared and the temperature subsided slowly with chemotherapy. Neurological examination failed to reveal a cause for the total loss of anal sphincter tone.

The patient continued to have complete urinary and fecal incontinence from the rectum which despite vigorous nursing care contributed to a progressive excoriation and inflammation of the perineum and buttocks. The patient had a mild fever attributed to the perineal cellulitis. Episodes of nausea and vomiting were frequent and loss of weight was marked. The nonprotein nitrogen remained normal throughout this period and there was no costovertebral angle tenderness or pain. Excretory urograms (fig. 1) remained unchanged. Frequent transfusion of whole blood and infusions of intravenous fluids were necessary to maintain nutrition and fluid balance.

By the latter part of October 1949 he had developed several ischiorectal abscesses which were incised and drained. After 5 months there was no evidence of return of anal sphincter tone and the recurrent abscesses in the buttocks and perianal region became more difficult to control. The incontinence had rendered the patient a complete invalid and his general course was progressively downhill. Surgical intervention was considered urgent. At operation the urinary and fecal streams were diverted by severing the sigmoid colon at its junction with the rectum and bringing the proximal end of the sigmoid colon out through an incision in the left lower quadrant of the abdomen. In essence an abdominal

cleared after this more effective prosthesis was applied. The patient soon became thoroughly familiar with the routine care of the wet colostomy and was able



FIG. 2. Ileostomy cup with disposable plastic collecting bag shown in place over cutaneous ureterosigmoidostomy. Bag is supported by pouch attached to elastic belt which is not shown in photograph.



FIG. 3. Excretory urograms taken 4 months following establishment of a wet colostomy or 10 months following original bilateral ureterosigmoidostomy. Notice moderate bilateral hydroureter and hydronephrosis. Right ureter can be seen crossing left ureter.

to apply the disc without assistance. The disc remained in place water tight from 24 to 72 hours. The plastic collecting bags were changed 4 to 5 times a day and disposed of easily in the toilet by flushing (fig. 2).

GIANT MEDICAL CALCULUS AND CARCINOMA OF THE BLADDER

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The stone herein described is the largest vesical calculus on record successfully removed by operation; it is also the largest reported calculus co-existing with carcinoma of the bladder.

REPORT OF CASE

A man 64 years of age entered the Mary Imogene Bassett Hospital on November 8, 1940, because of the loss of 25 pounds in weight. Incidental complaints were frequency and difficulty in urination with 2 episodes of gross hematuria. Ten years previously edema of his ankles was noted and albumin was present in the urine. Otherwise the patient was in good health until the onset of the present illness. He worked as a machinist until 4 days before referral to the Hospital. The present illness began insidiously 3 months prior to admission with loss of weight and increasing fatigue. These symptoms were followed by advancing edema of the ankles up to the knees and increase in the size and prominence of the lower abdomen.

There were *no urinary symptoms until 2 months before hospitalization* when frequency and difficulty in urination were first noted. Frequency increased, nocturia ensued and finally only a small amount of urine could be voided at one time. Two episodes of gross hematuria occurred. Burning, smarting and stinging with urination were denied.

The man was pale, debilitated and cachectic in appearance. The skin was loose, dry and flabby; subcutaneous tissue was sparse. The heart and lungs were essentially normal; the blood pressure was 136 millimeters of mercury, systolic, 82 millimeters diastolic. The abdomen was protuberant in the lower portion and diffusely tender; the superficial inferior hypogastric veins were distended. A firm, symmetrical, stony hard mass was readily palpable, rising from behind the pubis to the level of the umbilicus (fig. 1). This mass filled the true pelvis and could not be dislodged by manual manipulation. The prostate was normal. There were superficial varicosities of both legs and brownish pigmentation of the skin of the medial surfaces of the ankles.

When the patient was admitted to the Hospital the rectal temperature was 100.6 F., the pulse rate was 101 per minute and the respiratory rate was 24. Blood: The hemoglobin was 9.6 gm., the erythrocytic count was 4,300,000 per cubic millimeter, the leukocyte count was 46,700 with 70 per cent polymorphonuclear neutrophils, 12 per cent lymphocytes and 18 per cent eosinophiles. Urine: The reaction was alkaline, the specific gravity 1.007, albumin was present, the sediment contained numerous leukocytes and was loaded with erythrocytes; culture yielded *Pseudomonas aeruginosa* and *Proteus vulgaris*. Numerous subsequent examinations were similar.

The level of urea nitrogen in the blood was 12.8 mg. per cent, the level of calcium was 11.4, and of phosphorus was 3.75 mg. per cent; the acid phosphatase

Operation. The bladder was exposed extraperitoneally through a midline incision from the symphysis to the umbilicus. The properitoneal fat and areolar tissue of the prevesical space were indurated and edematous. When the anterior vesical wall was incised, a small amount of thick, malodorous urine was aspirated. The stone was firmly impacted in the bony pelvis, very adherent throughout the interior of the bladder and so large that it was impossible to apply both blades of an obstetrical forceps and still close the instrument. Consequently, one blade was utilized as a lever and the stone eventually delivered without undue trauma.

After removing the stone, the entire lining of the bladder was found to be inflamed, in places covered by thick sheets of fibrin and in others by what was thought to be cellular granulation tissue and shaggy fibrino-purulent exudate. Sections from several of these areas were removed for microscopic examination.



FIG. 3. Excretory urogram illustrating slight caliectasia and ptosis of right kidney with very little diodrast in bladder (compare with figure 2, 1).

Exploration of the vesical neck revealed some atresia of the prostatic urethra but no palpable evidence of prostatic carcinoma or of benign intravesical hypertrophy.

The bladder was closed around a large soft rubber tube brought out through a stab wound; the space of Retzius was drained with a cigarette wick, and the abdominal wall was closed in layers with catgut except for the skin, the edges of which were approximated with fine silk.

Five hundred cubic centimeters of blood were administered during the operation and the patient left the table in good condition.

Pathologic report. The gross specimen consists of a single, hard, greenish-white stone weighing 1110 gm. and measuring 14 cm. in its greatest diameter, 10 cm. in least diameter; the long circumference is 36 cm., the short 34 cm. Its shape is nearly spherical with a shallow groove extending halfway around and measuring 5 cm. in width (fig. 4). Over portions of the surface there are irregular small knobby elevations measuring 2 to 8 mm. in diameter and 2 to 6 mm. in height.

Also included are four sections of bladder wall measuring in aggregate 1 by

Pathologic diagnoses: Giant calculus of bladder, squamous cell carcinoma of bladder.

Roentgenogram of the stone showed it to be "made up of multiple concentric layers of calcification" (fig. 6).

An immediate marked febrile reaction occurred. The patient complained of feeling chilly but had no shaking chill, blood culture was sterile. The temperature and pulse rate subsided gradually to normal on the fifth post-operative day. A secondary febrile episode with actual chill followed 10 days later, blood culture was again sterile and the temperature soon returned to a normal level.

The suprapubic tube was removed on the sixth day and the bladder placed on drainage through an indwelling urethral catheter of the Foley type. However

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FIG. 6. Roentgenogram of stone after removal illustrating concentric nature of its structure.

urine continued to drain intermittently through the suprapubic vesical sinus. Bilateral epididymo-orchitis developed but responded to chemotherapy and antibiotics. The daily output of urine was normal and at no time was there clinical or chemical evidence of uremia. The abdominal wound healed satisfactorily except for the persistent urinary fistula which recurred whenever the catheter was removed.

Uterosigmoidal anastomosis and total cystectomy were recommended. The patient wished to go home for Christmas and was discharged on December 15, 1949, wearing an indwelling urethral catheter.

Summary of second admission: The patient returned to the Hospital for operation on December 27, 1949. During the interval at home he had been afebrile and asymptomatic except for one episode of vomiting, his appetite improved and he gained 4 pounds in weight.

Physical examination was essentially unchanged. The suprapubic wound was healed, however, soft abdominal distention and hypertympany were noted which had not been present when the patient left the Hospital 12 days previously.

stone in its moist state weighed 64 ounces, exactly 4 pounds. The patient died 36 hours after operation. Following a painstaking search of the literature Rindall concluded that this represented "the largest specimen of human vesical calculus formation of authentic record (certainly the largest removed during the life of the host) and a specimen so unique that it will probably stand in a class by itself for all time." Such has been true to date.

The largest stones of which record of *successful* removal can be found are those reported by Milton² from the Kasr-el-Ami Hospital in Cairo in 1893, by Smith³ from the Royal Victoria Hospital in Montreal in 1919, and by Lepreau and Jenkins⁴ from the New Haven Hospital in 1943.

The first of these² weighed one hour after its removal 995 grams equal to nearly 2 pounds, 2½ ounces, its largest diameters were 4 inches and 6 inches. The author stated that the success of the operation may be open to criticism from the fact that the patient died in the hospital from kidney disease and that at the time of his death he still had an urinary fistula, the result of the operation. Taking into consideration, however, that death took place 2½ months after operation, that during this period lithotomy was performed a second time for a new stone of renal origin, and that between the period of the second lithotomy and the time when the kidneys finally failed, the patient had a distinct period of *convalescence* and that he was about in the garden of the hospital, it may be claimed that although the operation failed to cure the incurable secondary changes in the kidney which resulted from the prolonged presence of the stone, the stone itself was successfully removed."

The second of these giant calculi³ successfully extracted by operation weighed 1455 gm. or 2 pounds, 9 ounces. It measured 9.6 by 14.2 cm. with a circumference of 36 cm. This patient left the hospital about 2 months later after the wound had been opened, a small additional calculus removed from the bladder and debris washed out. A pin point vesico-abdominal sinus persisted, drained at intervals, and required secondary closure 5 months later. The patient was well when discharged from the hospital 2½ months thereafter.

The third giant stone⁴ removed by Lepreau and Jenkins weighed 1134 gm. or 2 pounds, 8 ounces (measurements not given). This patient was well 2 years after operation. The investigation of the literature included in the report by the authors was conducted through the Yale Medical Library with microfilm material obtained from other sources, notably the Army Medical Library and the New York Academy of Medicine. As a result of this search this stone was believed to be the largest bladder calculus removed with complete recovery that had been recorded up to that time.

No report of a larger calculus successfully removed has been found during the intervening 6 years. The calculus herein described weighed 1410 gm. or 3 pounds, 2 ounces. The success of this operation, like that of Milton, may be open to question because the patient died 3 months later. However, death was due to advanced carcinoma of the bladder with metastases and not to the calculus or the

² Milton, H. M. N., *Lancet*, 2: 687-688, 1893.

³ Smith, I. C., *Surg., Gynec. & Obst.*, 29: 481-484, 1919.

⁴ Lepreau, Frank J. Jr. and Jenkins, R. H., *New Eng. J. Med.*, 229: 937-938, 1943.

INDICATIONS FOR THE NEUROSURGICAL ESTABLISHMENT OF BLADDER AUTOMATICITY IN PARAPLEGIA

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Our proposal is the development, by neurologic surgery, of an automatic bladder which is consistent with renal health and social compatibility. Rhizotomy from L12 to S5¹ or differential sacral neurotomy^{2,3} can accomplish this goal in a number of paraplegic patients. Such an automatic bladder must be predictable by test before neurosurgical intervention. The preoperative urological appraisal should rule out mechanical obstruction because of prostatic or bladder neck hypertrophy for which transurethral surgery may be indicated.

Relaxation of the perineal muscle group is essential for the initiation of micturition. A spastic perineum holds the orifice of the bladder high while the sensory nerve endings within the posterior urethra are stimulated by spasm.^{4,5} The result of this situation is bladder obstruction with frequent voidings. Ultimately retention may result in stretching and thinning of the bladder wall which interfere with adequate detrusor action. Interruption of the sacral reflex arc by rhizotomy or by sacral neurotomy, eliminates the spasticity of the perineal muscles. The relaxation lowers the dependent use of the bladder orifice and therefore lessens the necessary degree of perineal muscle lowering action.^{5,6}

Dissection of the spinal cord eliminates central control of the bladder. A secondary center in the sacral cord, governing the bladder through the sacral reflex arc, may then take charge of bladder function. It is the aim of Munro's ingenious method of bladder "training" to bring this secondary center into play and to produce a reflexly functioning bladder. There remains a fairly large number of paraplegic patients in whom tidal drainage and bladder training fail to reach or to maintain this goal.

While mechanical obstruction is a cause of a nonfunctioning reflex bladder, it can readily be overcome by transurethral surgery,^{7,10,11,12,13,14} a dysfunction

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¹ Meierowsky, A. M., Scheibert, C. D. and Hinchey, T. R. *J. Neurosurg.* 7: 33-38, 1949.

² Meierowsky, A. M., Scheibert, C. D. and Hinchey, T. R. *J. Neurosurg.* 7: 39-43, 1949.

³ Meierowsky, A. M. and Scheibert, C. D. *Exper. Med. & Surg.* 8: 437-448, 1950.

⁴ Parker, M. M. and Rose, D. K. *Arch. Surg.* 34: 828-838, 1937.

⁵ Rose, D. K. *J. Urol.* 26: 91-105, 1931.

⁶ Rose, D. K. *J. Urol.* 57: 579-598, 1947.

⁷ Munro, D. and Hahn, J. *New Eng. J. Med.* 212: 229-230, 1935.

⁸ Munro, D. *New Eng. J. Med.* 236: 223-235, 1947.

⁹ Bumpus, H. C., Jr. *J. Urol.* 57: 300-303, 1947.

¹⁰ Bumpus, H. C., Jr., Nourse, M. H. and Thompson, G. F. *J. A. M. A.* 133: 366-370, 1947.

¹¹ Emmett, J. I. *J. Urol.* 53: 545-564, 1945.

¹² Emmett, J. I. and Dunn, J. H. *Surg. Gynec. & Obst.* 83: 597-612, 1946.

¹³ Emmett, J. I. *J. Urol.* 57: 29-41, 1947.

¹⁴ Thompson, G. F. *U. S. Nav. Med. Bull.* 45: 207-214, 1945.

In approximately 100 cases which have undergone sacral block studies¹⁸ and in a group of 15 sacral neurotomies,¹⁹ a combination of S 3 and S 4, and a combination of S 2, S 3 and S 4 has given the most satisfactory results. Blocking of S 2, S 3 and S 4, of S 2 and S 3, and of S 2 and S 4 may also be tried. In isolated instances, one of the latter combinations may give a better result.

To avoid any possible error in interpretation, the indication for sacral neurotomy for the purpose of establishing bladder automaticity should only be made on the basis of repeated bilateral injections of novocain into the same combination of sacral nerves. In the presence of a cystoscopically normal bladder neck, micturition under excessive straining, a varying degree of residual urine or incontinence represents as much of a contraindication to sacral neurotomy as to rhizotomy.

Technique of sacral block. The second sacral foramen is situated one finger breadth below the inferior border of the posterior superior iliac spine, and about one fingerbreadth medially. The third sacral foramen lies $1\frac{1}{2}$ fingerbreadths inferiorly to the second foramen. The fourth foramen can be found $1\frac{1}{2}$ fingerbreadths below the third but is situated more medially. The fourth sacral foramen is rather shallow. No. 20 spinal needles are introduced bilaterally into the respective foramina by angling them at 45 degrees. They can be felt to fall into the foramen to a depth of one centimeter or more. The position of the needles can readily be verified by x-ray. Two to three cubic centimeters of fresh 2 per cent novocain are then introduced through each needle, and the needles are withdrawn.²⁰

Bladder studies. For all practical purposes, determination of bladder capacity, ability to void, and the amount of residual urine before and after the block, will give the examiner the necessary information to determine the indication for rhizotomy, or for sacral neurotomy, and to eliminate those patients in whom these methods are not applicable. It is essential that all bladder studies be completed within forty-five minutes of the onset of the nerve block. For our purpose we have found the following method of study practical and expedient.

A) Control study. Two hours after the catheter has been removed, the patient attempts to void in a sitting position. The urinary output is measured and the patient is catheterized in a supine position in order to determine the amount of residual urine. With the bladder empty, sphincterometrographic readings are obtained by pulling the catheter out into the urethra. Using a Munro tidal drainage apparatus as water manometer and fluid reservoir, G₂ solution is slowly introduced into the urethra and the pressure at which the fluid breaks through the sphincter is recorded.

Sphincterometrographic studies are immediately followed by a cystometrogram. In carrying out the latter, we have found it practical to use the Munro tidal drainage apparatus again as water manometer and fluid reservoir. So as not to use more than 20 minutes for the cystometrographic procedure, G₂ solution warmed to body temperature is introduced into the bladder at a rate of 300 drop

¹⁸ Schiffert, C. D. Studies on sacral reflex arc in paraplegia. IV. Analysis of total and differential block studies. In preparation.

¹⁹ Meirowsky, A. M., and Schiffert, C. D. Unpublished data.

²⁰ Pitkin, G. P. Conduction Anesthesia. Philadelphia: J. B. Lippincott Co., 1940.

gastrostomy had been substituted for a perineal one. The proximal sigmoid anastomosis was closed and inverted with two rows of sutures. The perineal abscess was benign. The perineal abscesses and sinus healed completely. The abdominal wound was kept as clean as possible by drainage and continuous suction. Despite this measure, there was moderate infection of the skin about the sigmoidostomy, and delayed healing of the wound about the stump of the sigmoid. The patient remained afebrile



REPRESENTATIVE CASE

W. H., a 32 year old male veteran, was wounded by shrapnel while in combat in Germany in September 1944. The injury resulted in a physiological transection of the spinal cord below the eighth thoracic dermatome. Laminectomy was performed on December 28, 1944, and again on September 18, 1946. There has been no return of sensory or motor function since injury. The patient developed moderately severe spasticity of all muscle groups below the level of physiological transection. The degree of spasticity has been stationary for the past 2 years. While the spasms of the lower extremities were moderately severe they did not interfere with ambulation and rehabilitation, and did not necessitate rhizotomy on that account. Upon graduation from watchmaker school, the patient entered the Neuro-surgical Section, Kennedy Hospital, in September 1949, for bladder studies and subsequent sacral neurotomy.

A suprapubic cystostomy was performed shortly after injury and allowed to close at a later date. The patient then used an indwelling urethral catheter. On June 18, 1947, a vesical calculus was removed and a transurethral resection of the bladder neck was done. Following this the patient was able to void, but the bladder capacity was not in excess of 100 cc due to bladder spasticity. A Cunningham clamp was worn to prevent incontinence. Intermittent urinary tract infections occurred.

Control cystometric study revealed a spastic bladder with a capacity of 110 cc and with incontinence and a residual of 10 cc (table 1). Differential sacral blocks revealed that bilateral S 3 and S 4 blocks gave the best results with relaxation of the bladder, decrease in sphincter tone, capacity in excess of 300 cc, no incontinence and easy voiding with a residual as low as 10 cc. Spinal anesthesia up to T 12 produced equally good results, but total lumbosacral rhizotomy was not indicated.

On September 30, 1949, bilateral sacral neurotomy of S 3 and S 4 was done with results duplicating those of the sacral block studies. One year after operation the patient is still voiding at will without incontinence and without residual urine. The patient passes as much as 400 cc urine at one time. No urinary tract infections have occurred.

SUMMARY AND CONCLUSIONS

In certain instances of paraplegia and quadriplegia, bladder automaticity can be established by anterior and posterior rhizotomy from T 12 to S 5, or by differential sacral neurotomy.

The indications and contraindications for neurosurgical intervention can be determined by execution of specific bladder studies under the influence of spinal anesthesia and sacral novocain injections.

The technique of these studies has been described in detail.

A representative case has been reported.

On this regimen the patient gained 21 pounds and his general health improved. Renal functions and the temperature remained normal during this three month postoperative period. It was possible by March 30, 1950, four months after operation, to rehabilitate this patient completely. He is now asymptomatic and he manages his cutaneous ureterocolostomy with facility.

There have been two short episodes of acute pyelonephritis during the past 18 months which responded promptly to penicillin and sulfadiazine on one occasion and aureomycin on the other. At present he is maintained on sulfadiazine 6 gm. a day without any ill effects. He evacuates solid feces 2 to 3 times per day. During the remainder of the time almost clear urine averaging approximately 2500 cc. per day drains from the colostomy.

Postoperative excretory urograms on February 21, 1950, revealed good bilateral function with moderate dilatation of both ureters and pelvis. It was further noted that following the end sigmoidostomy the right ureter crossed over the left ureter as illustrated (fig. 3). Recent x-rays revealed no evidence of metastases.

SUMMARY

A unusual complication following radical surgery for carcinoma of the bladder and a satisfactory method of treating this complication have been presented. It is concluded that the creation of an abdominal uretero-sigmoidostomy is a safe procedure and that the condition is compatible with normal physical

plane. It is slightly curved, its concavity pointing anteriorly. The contours are smooth. During injection the lumen is contracted and narrow and the collicular relief is always visible (fig. 1). During micturition the prostatic urethra dilates



FIG. 1. Normal case. Both pictures in exactly same oblique view. During injection, *A*, contracted prostatic urethra with smooth contours. Collicular relief and internal urethral orifice are seen. During micturition, *B*, widening of lumen of posterior urethra, change of shape of bladder and sinking of pelvic floor.



FIG. 2. Normal case, during injection. Contracted prostatic urethra, distinctly marked internal urethral orifice and interureteric ridge.

passing with a broad lumen into the bladder cranially, and into the membranous portion caudally. The colliculus is oval and protrudes into the lumen. The shadow of the moderately filled bladder is more or less oval and its long axis runs transversely to the body in frontal or oblique views. The base of the bladder is flat. With the patient in the recumbent position the internal urethral orifice

30 Gammex units and the alkaline phosphatase 6.8 King units; the total protein of the serum was 5.0 gm. per cent with 1.8 gm. as albumin and 3.2 as globulin.

Fluor. of the abdomen and lumbar spine disclosed a huge stone in the region of the bladder measuring about 14 cm. in diameter (fig. 2). Excretory urograms showed prompt excretion of the dye in good concentration by both kidneys. The calyces, pelvis and ureter on the left were relatively normal; the right kidney, however, the pelvis and calyces were slightly dilated; very little detail could be distinguished apart from the stone (fig. 3).



Fig. 2. Photographs of patient illustrating his cachectic appearance and prominent low back.

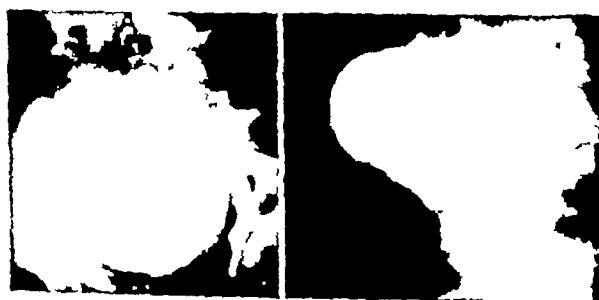


Fig. 3. A. Posteroanterior fluorogram of lumbar spine and pelvis showing shadow of calculus. B. Lateral film of calculus.

may be dilated during injection without showing a deformity or any other changes. In the less advanced cases the pericollicular urethra is widened while the remaining portion is normally contracted (fig. 3). In chronic cases, on the other hand, the prostatic urethra may be changed into a stiff tube which stands in broad communication with the membranous urethra and the bladder respectively, and the patients are incontinent. In such cases one may find numerous contrast-filled cavities and short dilated ducts close to the urethral lumen, also indicating an atrophy of the prostatic tissue. The bladder is often fibrotic in these severe cases.

From the point of view of differential diagnosis, in cases of cystitis a widening of the urethral lumen during injection may sometimes appear if distention of the bladder causes urgency. If the history is not known or is incomplete, a



FIG. 3. Case of prostatitis with atrophy during injection. Fairly pronounced dilatation of pericollicular urethra without deformity. Contrast filling of small glandular cavities in prostate.

widening after electroresection or removal may give rise to an incorrect diagnosis as well.

In most cases of prostatitis the prostatic urethra appears of normal length and shape on urethrocytograms. In some, however, the contrast examination may show an elongation of the supracollicular portion, the lumen of which is normally contracted and smooth (fig. 4). In addition, there may be a slight smooth protrusion into the bladder base. The collicular relief is intact, or swollen, and during micturition the dilatability of the prostatic urethra is normal. This urethrocytographic finding can be explained by a diffuse inflammatory enlargement of prostatic tissue in subacute and chronic cases. In a true prostatic enlargement there is no deformity or dislocation of the urethral lumen. Inflammatory changes seem in some cases to mask even the adenomatous sign, if hypertrophy of the prostate is complicated by prostatitis. In this way may be explained the absence of a deformity of the prostatic urethra on urethrocyto-

1 to 2 cm. Portions of the tissue are unusually firm and white. The remainder is reddish white. Several surfaces appear to have mucosal lining.

Microscopic—Very little recognizable bladder mucosa remains and where it is present it is several times the normal thickness. The rest of the epithelium is



Fig. 1. Photograph of giant vesical calculus and golf ball to illustrate comparative size.

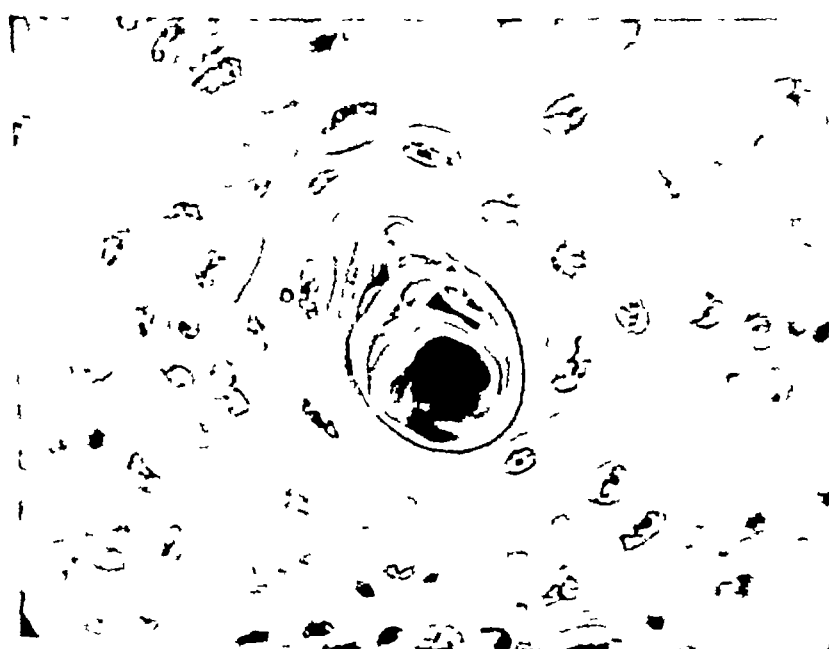


Fig. 2. Photomicrograph of wall of giant vesical calculus with Bulla of chondrocytes and chondrocytes. The outer wall is composed of a thick layer of chondrocytes and chondrocytes.

differential diagnosis in respect to cancer is difficult. In hypertrophy the unilateral displacement seems to be limited to the supracollicular portion, and a dislocation of the whole prostatic urethra is never seen. This is true even in advanced cases where the protrusions may be followed into the infracollicular region. Therefore localization of this feature to the upper part of the prostatic urethra, forming a smoothly outlined flat compression of the lumen from one side, indicates hypertrophy.

The collicular relief is most often deformed or not visible. In the bladder base there may be found one or more indentations of different sizes.

In some cases the only sign of hypertrophy may be a single adenoma at the internal orifice. The radiographs show a spherical protrusion into the most proximal portion of the urethra and into the bladder base. In addition, the



FIG. 5. Case of prostatic hypertrophy during injection. Typical picture of adenomatous enlargement with elongation and compression of prostatic urethra, angulation, and moderate bulging into bladder base. Contours are smooth.

frontal view during injection may show this portion of the urethra to form a delta due to spreading of the contrast medium at the lower surface of the adenoma. This finding of a spherical adenoma ("third lobe") is very important because of its valve action during micturition.

The contours of the urethral lumen and the bladder base in hypertrophy are smooth, with very few exceptions.

As opposed to hypertrophy, the growth of cancer is atypical, starting usually in the posterior lobe. The enlargement of the prostate is most often asymmetrical, and causes a deformity of the urethral lumen different from that produced by hypertrophy.

On plain radiographs the localization of calcifications may be studied according to rule. If these have a high position in the prostatic area or are situated in separated groups they may have been forced upwards or apart by tumor masses expanding from the posterior lobe (fig. 8). Osteoplastic metastases of the pelvic bones must be kept in mind as an important sign of prostatic cancer.

were caused by cancer only (fig. 8), while every adenomatous protrusion had smooth outline (fig. 5).

The differential diagnosis of hypertrophy and cancer is most difficult when hypertrophy is associated with cancer, which occurs in about 50 per cent of



FIG. 7. Case of prostatic cancer. Both injection, *A*, and micturition, *B*, pictures. Flattening of prostatic urethra with left posterolateral bulging into lumen and irregular contour.



FIG. 8. Case of prostatic cancer and hypertrophy during injection. Flattened, fluttered and angulated prostatic urethra. Flattening is interrupted in midpart and contours are irregular. Irregular bulging into bladder base. To right two groups of calcification, one before (upwards), other downwards, by expanding masses from posterior part of prostate.

cancer cases. In these instances the signs of hypertrophy may predominate on urethrocytograms, and the cancer be masked. If the cancer however has expanded to the prostatic urethra or grown into the adenoma, it may cause a deformity or displacement of quite a different nature or degree from pure hypertrophy and may be recognized.

true in spite of the fact that the incomplete contrast filling makes it impossible to study the shape of the orifice and the prostatic urethra. In such cases the radiologist must also bear in mind the possibility of a dysfunction of neurogenic origin.

Some of the cases with protrusion of a mass into the internal urethral orifice showed the most proximal portion of the urethra distinctly curved anteriorly and a little laterally, during the injection of contrast medium. It can be best studied in oblique views. In a frontal view the central ray is tangential to this proximal part of the lumen, giving a foreshortening of typical appearance.

As mentioned above, the so called "contracture of the bladder neck" may be a part of adenomatous or cancerous enlargement of the prostate. The true barrier without other roentgenological changes, occurs in prostatic cases. Then it may be confused with a single adenoma of a "third lobe" type. The differential diagnosis is based on the smooth spherical shape of the adenoma.

Cavities after removal or electroresection show typical urethrocytogram if the intervention has been performed correctly. After removal they have the appearance of a spindle shaped widening of the urethral lumen, whereas after electroresection they are funnel-shaped. The contours are often irregular. If surgical intervention has been incomplete, irregular contours may be the sole postoperative sign. This may result in a mistaken diagnosis of cancer, should the history be incomplete. The differential diagnosis also brings into question the condition of sphincter paresis, which may cause dilatation of the prostatic urethra similar to a postoperative cavity. Here, however, the case history is of greater importance. The paralytic widening is, in addition, always smoothly outlined. Finally, cases of cystitis may show a widened prostatic urethra due to violent urgency and immediate micturition when the bladder distends during injection of the contrast medium.

There is a very intimate functional correlation between the sphincter system of the prostatic urethra and the detrusor muscle of the bladder. Therefore a disturbance of the filling and emptying mechanism of the bladder, if neurogenic in character, should also be studied in both organs. As a detailed study of bladder lesions lies beyond the scope of this paper, the neurogenic disorders are not treated. The writer wishes to emphasize that the water-soluble contrast medium urethrocytography give a good view of the contraction or dilatation of the prostatic urethra and the size and the wall changes of the bladder.

In addition to the local changes previously described, the appearance of the bladder will be of value in the assessment of the functional importance of prostatic diseases. The bladder reacts to a chronic obstruction with dilatation of the lumen and hypertrophy of the detrusor. The longer the obstruction has lasted and the higher it is situated in the prostatic urethra, the more difficult is the emptying and the more pronounced the trabeculation and the diverticula formation of the bladder wall.

In using urethrocytography in the previously described manner, it is possible to combine in one examination a study of the changes of the urethra and the bladder base with a study of the bladder changes caused by prostatic disorder.

PRIMARY MALIGNANT NEOPLASMS OF THE SPERMATIC CORD AND EPIDIDYMS—TWO CASE REPORTS

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Primary malignant neoplasms of the spermatic cord and epididymis are considered among the rarest of all genito-urinary tumors.

In 1939, Schulte et al. were able to find only 247 spermatic cord tumors of which 30 per cent were malignant and 70 per cent benign.

O'Brien, in 1942, reported 92 cases of epididymal neoplasms of which 60 per cent were malignant and 40 per cent benign. He stated that there was some conflict as to whether most of the epididymal malignancies were sarcoma or carcinoma.

Secondary malignant neoplasms of both the spermatic cord and epididymis have occurred. Kenke in 1925 and Derm in 1927 reported secondary epididymal neoplasms from the kidney, as did Katzen in 1941. Lloyd Lewis et al. in 1944 reported a secondary invasion of both the cord and epididymis from a carcinoma of the stomach.

We have observed and operated upon a case of leiomyosarcoma of the spermatic cord (H. B.) and upon a case of leiomyosarcoma of the epididymis (B. S.).

Since these two structures have a similar embryological origin, a joint case report is presented.

Cribbree stated that tumors of the testicle and of the organs derived from the embryonic genital ridge cannot be considered entirely independently of each other. The latter group consists of the testicular tunics, the epididymides and the spermatic cord. It would therefore seem logical to expect a similar malignant neoplasm to arise in these tissues, and in the two cases to be presented a similar pathological lesion was found.

CASE REPORTS

Case 1. H. S., aged 66, a white man, was admitted on November 12, 1940 to Lebanon Hospital with a 6 weeks' history of enlargement of the right testicle. It was painless and not associated with urinary symptoms. He gave no history of trauma. The patient knew that he had a bilateral inguinal hernia for years and sought admission more for the repair of these defects than for the testicular swelling.

Examination revealed his heart and lungs to be normal. The blood pressure was 170/90. Abdominal examination revealed no abnormal masses.

A firm mass the size of a tennis ball was present in the right scrotum and appeared to involve the epididymis. It did not transilluminate and was non-fluctuant. The testicle itself felt free and the cord was not indurated. The left scrotal area and the penis were normal.

The prostate presented a grade 2 hypertrophy, was smooth and not nodular, fixed or tender.

testis showed a moderate degree of parenchymal atrophy. The lymph node did not show any evidence of metastatic involvement. Microscopic examination of sections from the vas showed infiltration of its outer coats by the tumor. Diagnosis: Leiomyosarcoma of the right epididymis (fig. 2).

A metastasis developed in the right humerus, as proven by biopsy in January 1951.

Case 2. S. J., aged 69, a white man, was admitted to the Jewish Memorial Hospital on November 27, 1945, and discharged on December 18 with the chief complaint of a painful right groin swelling of 3 weeks' duration which was getting progressively larger and more painful. He had had symptoms of prostatism for several years.

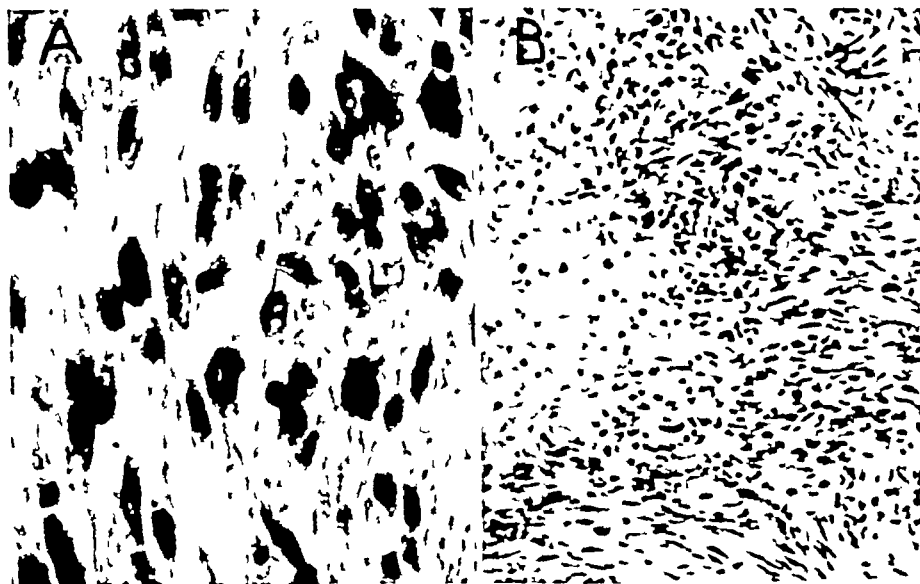


FIG. 2. Case 1. *A*, photomicrograph of epididymis showing marked variation in size, shape, and staining of nuclei $\times 300$. *B*, evidence of infiltration of local tissues by direct extension. Necrosis is present in several foci $\times 150$.

On examination, a hard mass the size of a tennis ball was present in the groin and was inherently attached to the spermatic cord. Further examination revealed normal heart sounds, no murmurs. The blood pressure was 112/70. The lungs were clear. Abdominally, no viscera masses or spasms were palpated. The penis was normal. Rectally, the sphincter tone was good. The prostate was grade 2, semihard and smooth. It was not fixed, tender or nodular. Residual urine was 1 ounce. The left testicle was normal, the right was moderately swollen and a small amount of fluid was present in the tunica vaginalis.

A preoperative diagnosis of malignancy of the right spermatic cord was made. At operation on December 3, 1945, performed by one of us (H. B.), the entire right spermatic cord and testicle were removed. The mass was found to extend almost the entire length of the spermatic cord from just above the testicle to 1 inch below the internal abdominal ring and appeared well encapsulated.

The patient returned on July 30, 1946 and was discharged October 8. He complained of a gradually increasing painless mass in the right groin associated with increasing urinary difficulties.

On examination an orange sized firm mass was found attached to the pubic right side of the symphysis and the root of the penis. X-rays of the chest and pelvis revealed no bony metastases or lung disease.

The entire mass was removed on August 7, 1946 and a careful groin dissection was also performed at this time. Following this operation patient developed increased urinary difficulties and could not tolerate a urethral catheter. His groin wound healed well and a suprapubic cystostomy was performed on September 6 by another staff member.

He received radiation therapy during this time, and on September 17 the radiotherapist (Dr. S. Rubinfeld) reported that during his present stay in the hospital the patient had received 2500 r to his right testicular and inguinal region enough to produce an erythema and some skin excoriation. Further treatment was to be continued after the second stage operation along the lymph drainage arc is up along the lumbar chain.

On September 23 a second stage prostatectomy was performed. His postoperative course was uneventful, and on October 3 deep therapy was resumed.

Pathological reports: 1) Prostate: cystic glandular hyperplasia and hypertrophy. 2) Region of spermatic cord: recurrent leiomyosarcoma.

Follow up x-rays of the pelvis and chest at this time revealed no metastases.

The patient was readmitted January 16, 1948 and discharged on February 3. At that time he complained of diarrhea, vomiting, and swelling of the right inguinal region. During the interim since his last discharge, he had been receiving intensive radiotherapy.

The patient appeared much weaker with an obvious loss of weight. His liver was enlarged and grossly irregular. A hard fixed mass was present in the right upper quadrant. A hard mass was also present in the right inguinal region under the previous scar.

The admission diagnosis was possible uremia, radiation poisoning, and generalized metastases.

An attempt was made to perform a cystoscopy but the posterior urethra was so rigid that it was impossible.

The radiotherapist felt that further radiation was inadvisable.

X-rays of the abdomen revealed evidences of hypertrophic osteoarthritides of the lumbar spine and increase in the size of the liver. Excretory urography revealed no visualization of the right kidney. The left kidney was normal. The chest revealed metastases to the left lung and its hilus. A gastro-intestinal series disclosed an epigastric mass which displaced the stomach anteriorly.

Urinalysis showed occasional white blood cells, otherwise normal, culture was sterile. The blood count disclosed moderate anemia, hemoglobin 70 per cent. The Wassermann test was negative. Chemistry: sugar 100 mg. per cent, urea 18 mg. per cent, creatinine 4.2 mg. per cent, alkaline phosphatase 9 King Armstrong units, acid phosphatase 1 King Armstrong unit.

mesodermal, 72 sarcomas and 3 carcinomas. Eighty per cent are classified fibrosarcoma or merely sarcoma. The remaining 20 per cent are composed of different mesodermal tissues as smooth and striated muscle, fat, bone, etc.

The treatment of spermatic cord tumors that are benign is simple excision. The generally accepted treatment of malignant tumors is removal of the testicle, epididymis, and cord as high as possible followed by deep x-ray.

The end results are still questionable but in the main are considered very poor.

Epididymal tumors. Neoplasms of the epididymis offer no characteristic features, and are greatly overshadowed in frequency by chronic inflammation, even syphilis. Exploration is the only method of establishing a diagnosis.

Hilpern in 1917 stated that 60 malignancies of the epididymis had been reported up to that time, and his case was the youngest, a child aged 3. The patient died in 1 year of generalized metastases.

Thompson stated that 75 per cent of epididymal malignancies have a 5 year survival, and that trauma seemed to stimulate the origin of many of the tumors. Most occurred in the latter decades of life.

Cheracke 1939 reported 22 benign and 54 malignant epididymal neoplasms up to that time, and stated that metastases was first by direct extension. Later metastases were like those of testicular tumors, i.e., lymphatic extension preceding venous invasion.

O'Brien in 1912 reported 92 cases of epididymal neoplasms of which 60 per cent were malignant and 40 per cent benign. Strong stated that 27 per cent of the malignancies were dead in less than 1 year.

Pathologically, there is still some conflict as to whether or not most epididymal malignancies are sarcoma or carcinoma. Statistically, both are equally distributed, only 2 per cent being teratomas.

The prognosis is much better than that of spermatic cord malignancies.

The treatment is the same as that for spermatic cord tumors.

Previous papers on this subject have been published by Hinman and Gibson, Lazarus, Mackay, and Thompson.

SUMMARY

The seventy-sixth malignant neoplasm of the spermatic cord is presented. The patient was in the latter decades of life and died 2½ years after the onset of symptoms of generalized metastases.

Most spermatic cord tumors are highly malignant, and our case was in keeping with this concept. There was only a 3 weeks' history, on admission, of a painful groin swelling.

Over 90 per cent of spermatic cord neoplasms are sarcomas. Our case was a leiomyosarcoma.

Despite radical surgery and intensive radiation therapy, generalized metastases developed.

The sixty-first primary epididymal malignant neoplasm is described. The patient, like our other one, was in the latter decades of life. The tumor was

FIG. 6. 11. In which the biopsy after electroresection or removal shows both glandular and epithelial hypertrophy.

If other conditions causing enlargement of the prostate are hypertrophy of the epithelium. The differential diagnosis will be discussed in the following paragraphs.

On plain radiograph hypertrophy must be assumed if calcifications within the prostate are displaced caudally and show a cup-like arrangement due to pressure from above. During urethrocytography contrast filled ducts may give similar information if they show the same displacement.

In agreement with the above mentioned calcifications. However most important for a cytological diagnosis of hypertrophy is the study of the prostatic tissue at the bladder base.



FIG. 6. 12. 12. In which injection of longitudinal supracollinear urethra with contrast medium is followed by formation of dilatation of lumen.

PRIMARY CARCINOMA OF MALE URETHRA: CASE REPORT

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P. M., a white man aged 58 years, was admitted September 27, 1945 complaining of general weakness and shortness of breath of 6 weeks' duration. Six weeks prior to admission he noticed blood in the urine and blood clots. He had frequency but no difficulty of urination. He gave no history of gonorrhea or of urethral stricture. He had never had urethral instrumentation.

Examination revealed an anemic, somewhat orthopedic individual. Crepitant rales were noted in the right chest posteriorly and a systolic aortic aortic murmur was noted.

The external genitalia were negative except for distinct induration of penis which extended from the bulbous portion to the distal $\frac{1}{3}$ of the penis (fig. 1, A). The prostate was slightly enlarged, elastic, and movable. Cystoscopy was attempted but introduction of the cystoscope was impossible. Such manipulation caused a continuous bloody discharge to exude from the urethra.

Biopsy was attempted through an open urethroscope but that too was unsuccessful. Biopsy of indurated area at base of penis revealed squamous cell carcinoma (fig. 1, B). A roentgenogram of the chest revealed a lymphogenous spread of metastatic malignancy (fig. 1, C).

Operation of any type was refused. The patient died October 17, 1945 and autopsy was refused.

1950 Chestnut St., Philadelphia 3, Pa.

The authors have recently published a complete review of the literature from 1891 to 1950 in which they have analyzed the history, physical findings, microscopic study, treatment and prognosis in 239 cases. (Urological Survey, 1: 1-30, 1951.) *Editor.*

CALCIFICATION OF THE VAS DEFERENS ASSOCIATED WITH PAGET'S DISEASE OF BONE

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Calcification of the vas deferens is an unusual clinical entity. Although it is rarely mentioned in the standard texts on urology, it has been previously reported in the literature. In 1942, Fowlsley and Ribboff¹ reported a total of 32 collected cases. Many of these cases, however, described calcification of the ampulla of the vas associated with calcification of the seminal vesicle. Calcification of the vas along its entire course, whether unilaterally or bilaterally, is less frequently seen. The etiology of calcification of the vas is not definite or constant. Henke and Lubarsch² in their discussion mention tuberculosis, gonorrhea, other chronic inflammations, senility, and diabetes as possible etiological agents. In diabetes, there may be an associated Monckeberg's arterial sclerosis as well as calcification of the vas. It is also mentioned that this calcification may be visible by x-ray and that there may be an associated calcification of the seminal vesicles. Pathologically, the calcification usually involves, and sometimes replaces the medial muscular coat of the vas, and microscopically closely resembles medial sclerosis of arterial vessels.

On the other hand, Paget's disease of bone, or osteitis deformans, is a very frequent clinical finding. It has been estimated to occur in 3 per cent of all autopsies in men over 40 years of age.³ The disease is appreciably less frequent in women. Since Paget's disease occurs in the older age groups in men, it is often seen in association with prostatic enlargement and obstruction. This becomes important clinically when x-ray differentiation between Paget's disease and metastatic prostatic malignancy is to be made. The etiology of Paget's disease is unknown. Biochemically, the serum levels of calcium and phosphorus are usually normal, and there is no hypercalcemia. However, this is not the fact when a patient with Paget's disease is immobilized for any considerable period. In this instance, hypercalcemia and hypercalciuria may occur and may be associated with urinary calculus formation. In Paget's disease, the alkaline phosphatase is usually quite elevated. Extrasosseous calcification is not associated with Paget's disease, but there is often premature and advanced arteriosclerosis.⁴

The unusual occurrence then, of advanced osteitis deformans and marked calcification of the vasa deferentia in a patient with prostatic obstruction, prompts the report of the following case.

JOHN, a 70-year-old white man, was admitted to the Mt. Sinai Hospital on November 18, 1950 with a 9-year history of intermittent, symptomless pyuria. Three years prior to admission he had had one episode of acute urinary retention.

¹ Fowlsley, O. S. and Ribboff, P. J. *J. Urol.* 47: 293, 1942.

² Henke and Lubarsch. *Handbuch der Speziellen Pathologischen Anatomie und Histologie*. Berlin: Julius Springer, 1941, vol. 3, p. 381.

³ Cecil, R. L. *A Textbook of Medicine*. Philadelphia: W. B. Saunders Co., 1947.

⁴ Sampson, J. *Medical Clinics on Bone Disease*. New York: Interscience Publisher, Inc., 1949.

and roentgenal diagnostic viewpoint irregularities of the lumen after the operation must be kept in mind as well. Where a complete resection has been performed the visualization of the postoperative cavity is an additional diagnostic sign. Incomplete intervention may cause a residual tumor in the absence of an accurate anamnesis.

Obstruction of the bladder neck may be caused by each of the above diseases as well as by congenital and neurogenic disorders. However, this is dealt in a special paragraph due to its clinical and roentgenological nature. The nature of this lesion is such that urethrocytography and cystography is ideally suited to demonstrate cases with a posterior bar



Fig. 1. A. Contracture of bladder neck during micturition. 1. Clinical symp. Circular contracture of internal opening with markedly decreased contrast. 2. Hyperplasia with bar formation. Bulging into internal urethral orifice. 3. Trabeculation of bladder wall also indicating

The penis and testes were normal but on both sides the vas was felt to be quite hard and beaded. On rectal examination the prostate was smooth and only minimally enlarged. The vesicles were not felt. On catheterization 15 ounces of puri-

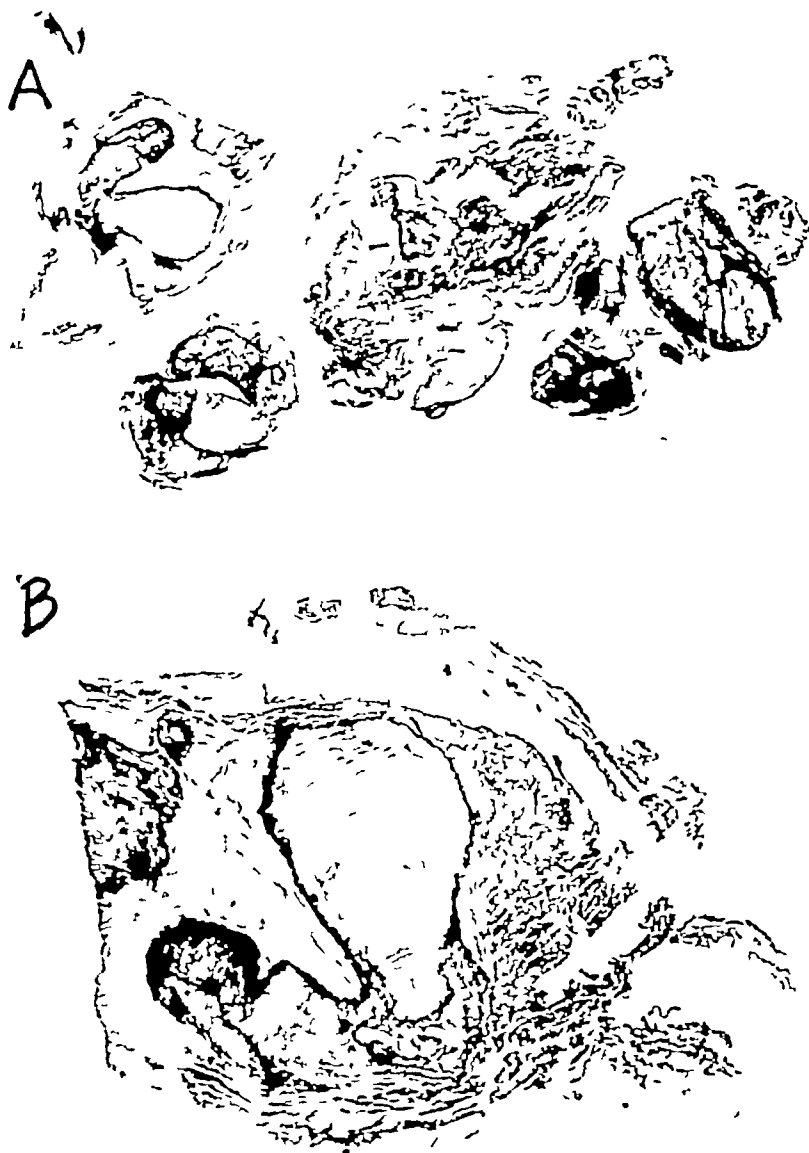


FIG. 3

lent urine were obtained after the patient had voided about 8 ounces. The catheter was left indwelling.

Urinalysis showed albuminuria and marked pyuria. Blood urea nitrogen was

Information given by urethrocytography relative to the morphology and the order of the lower urinary tract has been of greatest importance in the management of the patients and in their treatment.

SUMMARY

The author describes the urethrocytographic method and stresses the value of combination with a water-soluble contrast medium during both injection and retention, allowing a study both of the prostatic urethra and bladder and the bladder changes caused by a diseased prostate. In the paper are listed the roentgen signs of post-inflammatory changes, enlargement of the prostate due to prostatic hypertrophy and cancer, contracture of the bladder and finally the state of affairs after surgical intervention.

REFERENCES

UROGENITAL TUBERCULOSIS A REVIEW OF 209 SURGICALLY TREATED CASES

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Urogenital tuberculosis as an entity in a hospital solely devoted to the treatment of tuberculosis presents a problem entirely different from that in a general hospital or in private practice. The principal difference between these lies not in a different anatomic process, but rather in the fact that in most instances in a tuberculosis institution urogenital tuberculosis is secondary to and develops while the patient is under treatment for another form of tuberculosis (chronic pulmonary and skeletal tuberculosis).

The problem of the treatment in multiple system tuberculosis is often a complicated one, since in a number of cases there is an active tuberculosis of three organs, all requiring active treatment.

During an 18 year period (1931-1948) 209 cases of urogenital tuberculosis were subjected to either nephrectomy or epididymectomy, or both procedures. We have included those cases in which the operation was done at another hospital and admitted to our service for treatment of the draining sinus which followed the procedure. A nephrectomy was done in 63 instances, an epididymectomy (unilateral or bilateral) in 105 cases and in 41 patients an epididymectomy and nephrectomy were performed.

NEPHRECTOMY

In the 104 cases in which a nephrectomy was performed, the operation was done at our hospital in 73 instances and in 31 at another institution. These latter cases fall into two categories. One group (21) of cases reached our service for the treatment of a sinus tract following a previous nephrectomy, the other 10 for an epididymectomy for tuberculosis of the epididymis.

The right kidney was removed in 57 cases (54.8 per cent) and the left in 47 (45.2 per cent).

Sex. There were 81 (77.8 per cent) men and 23 (22.2 per cent) women. This is a greater proportion of men than in the entire population of the hospital during this period of time.

Race. Eighty-six (82.7 per cent) of the 104 patients were white, 17 (16.4 per cent) were Negroes and 1 (0.9 per cent) was Chinese. There is a greater proportion of whites in this series, since the patient population during this time was composed of 64 per cent whites.

Age. From table 1 it may be seen that 50.9 per cent of the patients are in the age period between 20 and 39 years. The youngest patient in this series is 10 years of age while the oldest is 63 years.

Associated skeletal tuberculosis. Active tuberculosis of the skeletal system was present in 24 (23.1 per cent) of the patients. In most instances renal tuberculosis developed while the patient was under active treatment for skeletal tuberculosis.

Urinary blood count and blood urea were normal. Wassermann was negative.

A preoperative diagnosis of bilateral indirect inguinal hernia and a malignant neoplasm of the right epididymis was made. The prostatic enlargement was felt to be benign.

On November 14, 1949, a right orchietomy, right inguinal herniorrhaphy, and excision of the inguinal nodes were performed by one of us (B.S.). At operation a tennis ball-sized tumor involving the right epididymis was present. It felt grossly malignant. Several enlarged lymph nodes were present in the right inguinal region. A right indirect inguinal hernia was also present. The patient made an uneventful postoperative recovery.

Pathological report (Dr. Joseph Ehrlich, director of Laboratories, Lebanon Hospital). The gross specimen (fig. 1) consisted of a right testis, epididymis,



FIG. 1. Gross specimen of right testis, epididymis, and spermatic cord.

was dependent upon the clinical signs mentioned above and the presence of tubercle bacilli in the urine. In three instances where the latter findings were the basis for a nephrectomy, the tuberculous process within the kidney was found within the kidney as an area of caseation (2-4 mm) which had softened and ruptured into a renal tubule.

Pathologic findings The tuberculous process varied from that of small tuberculous foci in an apparently normal appearing organ to one in which the kidney was greatly enlarged and almost completely occupied by tuberculous cavities.

The minimal cases are those in which the tuberculous process is limited to small cavities in the apical portion of the pyramid, usually the superior one. The calyx in this region often shows superficial ulceration.

The remainder of the cases may be divided into those in which following the complete occlusion of the ureter the entire kidney is converted into oval and round cavities varying in diameter from 2 cm. to 4 cm. The walls of the cavities are from 2 to 3 mm. in thickness. The lumina of these cavities are at first filled with soft, liquefied, caseous material rich in tubercle bacilli. In those instances where obstruction has been present for longer periods of time the caseous material became dry as a result of the absorption of water. This process has been termed "autonephrectomy." The bladder in these cases often shows no evidence of tuberculous ulceration since tubercle bacilli cannot reach it. Partial obstruction of the ureter over a longer period of time may result in a greatly enlarged kidney.

Outcome There are 47 individuals who died in a period of from 1 day to 13 years after the operation. The remaining 57 cases are known to be alive from 4 months to 17 years.

GENITAL TUBERCULOSIS

In the 146 cases of epididymectomy for tuberculosis there were 93 upon whom a unilateral operation was performed and 53 where both epididymides were removed. In most instances the epididymectomies were performed at different times, in a few instances they were done at the same time. The operations were performed in our institution on 133 patients, and in the remaining 13 the patients were admitted for the repair of a sinus tract following such an operation at another institution.

Race There were 113 (77.4 per cent) whites, 29 (19.9 per cent) Negroes and four (2.7 per cent) Asiatics. This closely parallels the race incidence of male genital tuberculosis in our autopsy series where a complete study of the genital system is possible.

Age Table 1 shows that genital tuberculosis is a disease which becomes prominent after the second decade of life. The youngest individual in the series was 14 years of age and the oldest 67 years. The greatest number of cases in this series was in the age group between 40 and 49 years.

Associated skeletal tuberculosis In 36 (24.6 per cent) cases there was an active skeletal tuberculosis. As in renal tuberculosis the skeletal tuberculosis preceded the development of genital disease in the great majority of instances.

Associated pulmonary disease The close relationship between genital and pulmonary tuberculosis may be seen from the fact that chronic pulmonary

that Thomas et al¹ in a study of renal tuberculosis at an institution treating all forms of tuberculosis found associated bone tuberculosis in 10 per cent of their cases and clinically active pulmonary tuberculosis in 62 per cent

The development of urogenital tuberculosis during the course of chronic pulmonary and skeletal tuberculosis speaks for a hematogenous dissemination from the latter two systems to the renal and genital organs

The successful treatment of urogenital tuberculosis will then depend in great extent upon the successful treatment of the extra-urogenital tuberculosis There are two main reasons for this 1) As long as pulmonary or skeletal tuberculosis remains active the possibility exists that further seeding to the opposite kidney or in genital tuberculosis of new foci developing on the same or opposite side This is amply demonstrated in the cases where the tuberculous process was removed on one side (nephrectomy or epididymectomy) and sometime later a new tuberculous disease developed in the opposite Braasch² in his series observed that when bilateral renal tuberculosis occurred, in the majority of cases the second kidney became infected several years after the first one

One may raise the question as to possibility of the fact that the foci were seeded to both sides, at the same time, but that progression to organ tuberculosis occurred in one kidney and that some time later (after nephrectomy or epididymectomy) the previously seeded foci in the opposite organ underwent progression or reactivation Against this latter point of view is the fact that the foci developing in these organs are of different anatomic age and that they are all more recent than the active pulmonary or skeletal tuberculosis, indicating multiple seedings Another important fact is that foci present for any length of time show extensive healing changes, and in none of the early cases have we observed reactivation of older foci 2) Extra-urogenital tuberculosis is often the cause of death in these cases

Age It is interesting to note that there is a rather parallel distribution in age groups between tuberculosis of the epididymis and the kidney In only 4.7 per cent of the cases of genital tuberculosis and 10.5 per cent of renal tuberculosis were the patients less than 20 years of age This is easily understandable since most of the cases in this series are secondary to pulmonary or skeletal tuberculosis which in the majority of instances are present after the age of 20 years Jeck³ in a study of 58 cases of renal tuberculosis from a large municipal hospital found an almost similar age distribution to ours and in his series also there were no cases in the first decade of life Kretschmer⁴ in a series of 94 cases of tuberculosis found the peak involvement in the fourth decade while ours occurred in the third

We believe that there is another factor which plays a role especially in male genital tuberculosis Auerbach⁵ in a study of genital tuberculosis found a greater incidence in females than males below the age of 20 He thought that the reason for the more frequent occurrence in younger females lay in the fact that there

¹ Thomas G J Kinsella, T J, Petter C K and Stebbins, T L J Urol 39 766-773 1938

Braasch W F J A M A 18 397-401, 1912

² Jeck, H S J A M A 92 300-306 1929

³ Kretschmer H I Am J Surg 9 221-229, 1930

⁵ Auerbach O Quart Bull Sea View Hosp, 7 188-206 1942

disease. Much confusion still exists on this important factor, for if both kidneys are involved nephrectomy will be of no avail.

It is a generally accepted view that renal phthisis is the result of a hematogenous tuberculosis, yet two factors must be explained. 1) Renal phthisis in the vast majority of cases is unilateral, whereas one expects most cases to be involved bilaterally and, 2) in most cases observed clinically and in many anatomic reports, the early tuberculous lesion is present at the apex of the pyramids, whereas in hematogenous tuberculosis the tuberculous foci should be present predominantly in the cortex.

Serial sections of kidneys in cases of chronic pulmonary tuberculosis without clinical evidence of renal tuberculosis by Medlar¹⁵ and Band¹⁶ have shown a high percentage of small tuberculous foci (some with a caseous center) usually in both kidneys.

That individuals with active tuberculosis of an extrarenal organ may show repeated hematogenous seedings in the kidneys is evidenced by the finding of these tuberculous foci in various stages of anatomic development. What is the relationship between these hematogenous seedings which are frequent, and renal phthisis, which is infrequent and why with frequent hematogenous seedings does not renal phthisis develop more often? The explanation perhaps lies in the structure of the kidney.

When tubercle bacilli gain a foothold in the kidney the resultant foci are either purely cellular or contain a caseous center. The smaller tend to be cellular and these go on to anatomic healing and result in fibrous tissue scars. The caseous foci (generally the larger ones) are the important ones in the production of tubercle bacilluria or the production of renal phthisis. The bacilluria is produced by the rupture of the tubercle bacilli into the lumen of a renal tubule and their subsequent passage through the uriniferous system into the calyces.

Renal phthisis may develop subsequently either through the direct rupture of a medullary caseous focus directly into the calyx, or superficial ulcers may form at the apex of the pyramids or in the calyx walls as a result of the tubercle bacilli which land in these areas after excitation of the tubercle bacilli following the liquefaction of the caseous foci and rupture into the uriniferous system.

The great tendency for hematogenous foci to become encapsulated or organized, the slight tendency of caseous foci to rupture into the tubules, and the low incidence of hematogenous caseous foci at the apices of the pyramids, so that rupture of the latter into the calyx will result in ulceration of the pyramids account for the low incidence of renal phthisis and its restriction to one kidney in the majority of cases.

The tendency to unilateral renal tuberculosis is well demonstrated in our series where only 13 showed bilateral involvement. Our findings at autopsy in which most of the cases are nonsurgical also showed a preponderance of unilateral cases. Our findings definitely substantiate the views of Wildbolz¹⁷ that renal tuberculosis is usually a unilateral disease.

¹⁵ Medlar J. M. *Am J Path*, 2: 401-413, 1926.

¹⁶ Band D. *Edinburgh Med J*, 42: 162-174, 1935.

¹⁷ Wildbolz H. *J Urol*, 21: 145-179, 1929.

comparable and almost an incidental finding, the patient complaining only of pain.

The pathology was leiomyosarcoma.

Approximately 50 per cent of such neoplasms have been reported as carcinoma.

Metastases of these tumors are similar to those of testicular tumors, i.e., to the lymphatics first.

It is too early to prognosticate concerning our case, but a 75 per cent 5-year survival for all such neoplasms has been reported.

CONCLUSION

Malignant neoplasms of the spermatic cord and epididymis are very rare.

The twenty-sixth case of spermatic cord malignancy and the sixty-first case of epididymal malignancy are presented.

Pathologically, both were pathologically leiomyosarcoma.

Statistically, over 90 per cent of primary spermatic cord malignancies are sarcoma.

Statistically, only 50 per cent of primary epididymal tumors are sarcoma.

A 75 per cent 5-year survival period of epididymal malignancies has been reported.

Primary neoplasms of the spermatic cord are much more serious.

Pathologically, the spermatic cord and epididymis have the same malignancy, but differ in the types of malignancies affecting each and their prognoses, requiring observation.

A review of the literature is presented.

Radical surgery seems to offer the best prognosis. The role of radiation therapy is not known.

There are 104 (49.9 per cent) of the patients who are known to have died. In this group are 31 upon whom a nephrectomy was performed, 57 upon whom a unilateral or bilateral epididymectomy was done and 16 upon whom both a nephrectomy and epididymectomy were performed.

TABLE 2 *Cause of death*

	NEPHRECTOMY	EPIDIDYMECTOMY
1 Chronic pulmonary tuberculosis	17	39
2 Uremia (renal tuberculosis in other kidney)	13	9
3 Uremia (amyloid)	4	5
4 Tuberculous meningitis	2	8
5 Tuberculous peritonitis	2	3
6 Acute miliary tuberculosis	2	5
7 Laceration of pleura	1	—
8 Excess sulfathiazole	1	—
9 Congenital hydrocephalus	1	—
10 Postoperative death	1	—
11 Blow out of renal artery stump	1	—
12 Cause unknown	2	—

Some interesting observations can be made by the comparison of both groups (table 2). There were 3 deaths in the nephrectomy series which were directly related to the operation. In one instance the ligature of the renal pedicle loosened after 3 days and the patient died of a fatal hemorrhage into the abdominal cavity. In another case the diaphragm was torn during the nephrectomy and although it was repaired, a large opening subsequently developed in the diaphragm. A suppurative inflammation developed in the pleural space and in addition the intestinal viscera extended into the pleural cavity. The patient died 3 months after the operation. The third case was one who went into shock just after the operation and died the next day.

There was no death related to the operation in the cases of epididymectomy series.

The chief cause of deaths in both groups is chronic pulmonary tuberculosis which is to be expected since it is the most common accompaniment of urogenital tuberculosis. The much greater frequency of pulmonary tuberculosis as the cause of death in genital tuberculosis is the fact that the latter more frequently accompanies the former.

The second most frequent cause of death in both the nephrectomy (27.7 per cent) and the epididymectomy (12.3 per cent) series is uremia on the basis of renal tuberculosis. In all of the nephrectomy cases the renal tuberculosis in the opposite kidney was extensive. In 4 of the 13 cases bilateral renal tuberculosis was present at the time of the nephrectomy. The kidney with the more advanced tuberculous process was removed with the view that a nephrostomy on the opposite side may be of some aid to the patient. The three cases were performed early in our experience with this disease. We are in complete agreement with views of Calk,¹⁴ Wildbolz,¹⁵ Beer,²⁵ and Kretschmer⁴ that patients with bilateral

¹⁴ Calk, J. K. *J. Urol.* 26: 189-201, 1931.

²⁵ Beer, I. *J. A. M. A.* 92: 1912-1917, 1929.



FIGURE 1. LIOMYX CARCINOMA OF MALL UPITHPA.

THE USE OF STERILIZABLE GOGGLES IN CYSTOSCOPIC AND TRANSURETHRAL PROCEDURES

JOSEPH H KIEFER

In the development of present cystoscopic technique, one thing has never been adequately provided, and that is the maintenance of sterility of the instruments throughout the procedure. Although perfectly sterile at the start of the examination, contamination occurs in a short time, due to contact of the instrument with the operator's face or eye glasses.

This is not so important in the case of a simple examination, and its bad effects can be avoided by precise technique, in ordinary cystoscopic manipulations. However, in the course of a lengthy procedure, such as resection of the prostate or of bladder tumors or ureteral manipulations, it is practically impossible to avoid contamination of the instrument, with transfer to the hands and thence to the entire field.

Various attempts to solve this problem have been made. The late Hugh Young put a separate collar on his cystoscope so that the hands need not touch the eye piece. Even so, in the interchange of telescopes which occurs in any lengthy procedure, constant and meticulous attention is required to prevent contamination.

We believed that if a sterilizable shield could be used to prevent contact between the face and the eye piece of the instrument, the problem would be solved. We contacted several makers of industrial goggles and shields and tried out a number of their products, which on first examination looked like they might work. The overall face shield is too cumbersome. The closed type of goggle was unsatisfactory since there was fogging of the surfaces. The shield which finally turned out to be most practical was a light plastic protective goggle (fig 1).

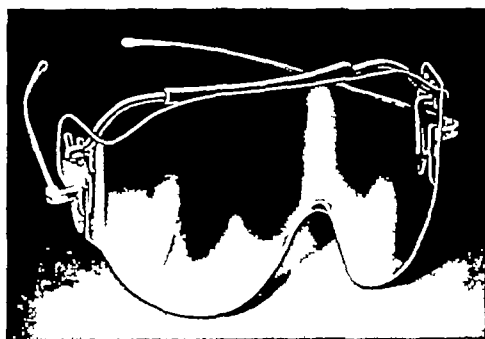


FIG 1

This is large enough to prevent contact of the face with the instrument under ordinary conditions. The goggle fits over ordinary eye glasses. The temple pieces are straight so the goggle is easily put on by the wearer alone without contamination.

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which had been treated by an indwelling catheter for a short period. Since that time, except for recurring pyuria, the patient's urinary symptoms had been absent. He also gave a history of a gradual increase in the size of his head of



FIG. 1



time If the glomerulus works, it must filter the liquids of the blood in order to form urine, if the glomerulus does not work, no blood at all must pass, because, even if it is very little that passes through, some urine must always filter, and then it already interrupts its rest to recover its function and to secure its anatomy. If it stops working, producing contraction, so to say, of the afferent artery thus not allowing the blood to flow into the glomerulus, the metabolism of all the tubules of this arterial portal system of the efferent artery is endangered. Let us not forget that the renal artery has no anastomosis and therefore, the tubule that is irrigated by the efferent artery of the correspondent glomerulus is a tubule that has no other element for metabolical interchange than the blood that such a vessel conveys. This contraction and occlusion arterial system could seem secured by the sphincterian mechanisms of Oberling and Bensley, but, if we look for them carefully in the respective vessels, we shall see that they are not so easily found, it could simply be the wall of the vessel that has been found in contraction and that shows a slight thickness, since in other vessels, even in those of the same preparation, we do not find such thickness. Nevertheless, this can not secure the emptiness of the glomeruli, because, even in the case of the contraction producing itself in the afferent, it would not secure, either, the evacuation of the glomeruli of the elements that are in it so the rest that must exist in all glomerular elements would also be altered.

If we study the action of the neuro-stimulation drugs, either of parasympathetic or of sympathetic stimulation, we shall see how difficult it is to explain the action of these drugs in the functioning of the glomerulus.

We know, through experiments made by Richards (1933), that small doses of adrenalin enlarge the size of the glomerulus, producing what is believed to be vessel constriction of the efferent element, while large adrenalin doses produce contraction of the afferent, diminishing the size of the kidney. So, in this case, the kidney should be in ischemia and the blood flow through the vein should stop, but this does not happen in case any other antagonistic drug should be given, be it pilocarpine or amyl nitrite that, instead of producing vessel constriction, causes the arteries to relax, we see that, in both cases, the blood that flows from the renal vein is red as if it were arterial blood. That is to say, that it is blood which has passed through the kidney without absorbing the elements or catabolism and without charging itself with carbon dioxide and wasting the oxygen it carries. It is then difficult to imagine that this blood could have passed through a renal glomerulus without producing the filtration function of the organ.

Besides, physiologically it also happens that the blood that flows out through the efferent artery with loss of water and electrolytes, obtains such a viscosity that it would need a vessel of perhaps larger diameter than the afferent vessel, or with such a modification in its walls that would secure the subsistence of this vessel without its being hurt by this extraordinary increase in weight and osmotic tension determined by the superconcentration of the elements of the blood in the efferent vessel. Apart from this, the rate of blood flow would slacken through a vessel of less diameter and with a certain increase in viscosity, a much higher increase of viscosity than the efferent vessel should logically

Associated pulmonary disease The lungs were free of tuberculosis in 48 (46.2 per cent) cases. In 4 (3.8 per cent) of these cases a miliary tuberculosis was the terminal episode in the patient's life. In the remaining 52 (50 per cent) there was a chronic pulmonary tuberculosis of which eighteen (17.2 per cent) showed evidence of clinical arrest by the disappearance of the cavities in the roentgenograms and the tubercle bacilli in the sputum. In two other cases a miliary dissemination, which was part of a generalized hematogenous distribution, developed in the previously uninvolved portions of the lung parenchyma.

Complications In 40 (38.4 per cent) the operative procedure was followed by the occurrence of a sinus at the operative site and in one instance the diaphragm was cut inadvertently during the operation. Twenty-one of these were patients who had the nephrectomy performed at another institution. In the series of 73 nephrectomies performed at our institution a sinus at the operative site occurred 19 times (26 per cent). The development of the sinus in most instances was an

TABLE 1

A Age of patients with nephrectomy					
Age in years	10-19	20-29	30-39	40-49	50 and over
No. cases	11 (10.5%)	28 (26.9%)	25 (24%)	23 (22.2%)	17 (16.3%)
B Age of patients with epididymectomy					
Age in years	10-19	20-29	30-39	40-49	50 and over
No. cases	7 (4.7%)	29 (19.9%)	34 (23.2%)	40 (27.3%)	25 (17.1%)

immediate one in which the operative wound never underwent healing. In 4 instances, however, the sinus developed in from 3 months to 21 months after the operation. The skin opening varied from 1 mm. in diameter to one which was several centimeters in diameter.

Microscopically, the wall of the sinus tract in all instances was composed of tuberculous granulation tissue.

Operative indications. Signs and symptoms The most constant symptoms in the series were hematuria, frequency and nocturia. Others such as dysuria, lumbar pain, pyuria and urgency although present, were not as consistent as the first three.

It is interesting to note that in 9 instances there were no symptoms referable to the renal tuberculosis. Attention to this site was first drawn by the presence of acid fast organisms in the urine. The urine is examined routinely for tubercle bacilli in patients who have active skeletal or genital tuberculosis and in many instances of active chronic pulmonary tuberculosis where a hematogenous dissemination is suspected.

Duration of symptoms The interval between the onset of symptoms and the nephrectomy varied from 1 month to 5 years. The vast majority, however, were from 1 to 3 months.

Roentgenographic findings In most cases the tuberculous process within the kidney had advanced within the kidney to present no problem. Occasionally the findings were equivocal. In these instances, however, the decision to operate

anatomists as already existent in the kidney, have been greatly discussed. Trueta has given us lately the most true, categorical and absolute explanation. To Trueta, the formation of the "vasa recta vera" is simply due to glomerular sclerosis and to the joining of the afferent artery to the efferent, that establishes in this way a single vessel. Trueta's demonstration has an extraordinary importance in the findings that we ascertain. In pathological sclerosis processes of the glomerulus, the artery forms itself, that is to say, the apparent arteriole of a subdivided artery directly joins a venule without interposition of a glomerulus.

Another very important reason to doubt of the actual conception of the constitution of the glomerulus, is the deviation of the renal blood current found by Trueta in Bywater's and Beall's cases (1941) of crush syndrome. We all know that in these crush cases a state of renal ischemia is produced, and Trueta has been able to demonstrate that it is due to the absolute absence of blood flowing into the cortical glomeruli and to the diversion of the blood that flows through the renal artery and passes directly to the renal vein by means of a juxtamedullary system. This experiment, having been proved to be true several times through repetition of the crushing syndrome or through stimulation of the sciatic nerve or through the administration of neuro-stimulation drugs, tells us of the arterial relaxation, causes an increase of the caliber of the efferent vessels allowing the blood to flow easily, but the blood should undoubtedly pass through the glomerulus, according to the ordinary conception of the glomerular looping formation. Nevertheless, the anatomopathological preparations tell us about the glomerular ischemia. In order to demonstrate this experiment of short-circuit, Simkin, Bergman, Silver and Prinzmetal (1948) injected the animal submitted to the crushing syndrome, whether real or artificially, with small pearls that, entering through the renal artery, are directly received in the vein. We may observe that, even if the glass pearl is very small, it is impossible for it to pass through the glomerular loops, they will be forcibly stopped in them as they have no bigger diameter than 20 microns. Nevertheless, Simkin and associates have obtained pearls of 400 microns through the renal vein, so we ought to think that there must be something able to explain such a demonstrative and categorical experiment. Goormaghtigh's system could evidently explain this bringing back of the glass pearls as the diversion of the blood through the juxtamedullary glomeruli, and the renal ischemia, but, as we shall later on demonstrate, this system seems artificial and makes no sense.

TECHNIQUE

In our research work on glomerular structure in men and in our laboratory animals especially in rabbit and dog, we have employed the following technique: injection of the kidney with India ink, in order to be able to demonstrate the blood stream, and injection of sodium iodide so that radiography could be secured. We have also applied the corrosion technique in order to be able to demonstrate the shape of the glomerulus but, as we were not pleased either with the corrosion technique or with India ink injection or with simple sections, we have performed series of sections of the glomeruli to determine categorically the

tuberculosis was present in 70.6 per cent of the cases. In 24 (16.4 per cent) of these cases there was healing of the lung process in the form of closure of the cavities and the disappearance of tubercle bacilli from the sputum. The presence of a clear lung in 42 instances (28.7 per cent) and also the 4 cases in which a terminal acute military tuberculosis existed show that the great majority of cases of genital tuberculosis in this series are associated with chronic pulmonary tuberculosis.

Pathologic findings. In the early stages the epididymis is only slightly enlarged and the process is limited to the tail or head. Later, the organ enlarges to four or five times the normal size. The enlargement may be nodular or even

Cross section of the early stages shows slightly thickened tubular walls with purulent material exuding from the lumina of many tubules. Caseous foci develop in the center and gradually the epididymis is converted into a caseous mass. The scrotal sac is usually thickened and adherent to the epididymis.

Liquefaction within the caseous foci was often seen in our cases and in some instances where it was extensive it extended out through the scrotum and resulted in sinus tracts.

Complications. The operative procedure was followed by a sinus in 33 cases (22.6 per cent). Ten of these patients were admitted to our hospital with a scrotal sinus, after an epididymectomy at another institution. Their admission to this hospital was for the repair of the sinus. The sinuses occurred in from an incomplete healing of the wound to 6 months following the operation and in all but two instances followed immediately the operative procedure. The sinus tract in all instances was lined by tuberculous granulation tissue.

Operative indications. Enlargement of the epididymis was the indication for surgery in all instances in this series. In the majority of instances the swelling was painless and most often was first noted by the patient. There were a few instances in which the enlargement was first noted by the physician while the patient was under treatment for some other form of tuberculosis. In 28 of the cases the liquefied caseous epididymitis had perforated through the skin of the scrotum to form one or more sinus tracts.

Duration. The time between the onset of tuberculous epididymitis and the operative intervention varied from 1 month to 5 years. It is interesting to note that the time interval in most instances was from 1 to 4 months. This may be explained by the fact that the enlargement is readily noticeable by the patient.

Outcome. There are 73 individuals who died in a period of from 1 month to 13 years after the operation. The remaining 72 patients are known to be alive from 4 months to 17 years.

DISCUSSION

Extra urogenital tuberculosis. In an institution devoted to the care of tuberculosis patients, renal and genital tuberculosis in the majority of instances is associated with chronic pulmonary tuberculosis. This association is greater in genital tuberculosis. Concomitant skeletal tuberculosis, although less frequent than chronic pulmonary tuberculosis, is a frequent occurrence in urogenital tuberculosis, more so in genital than renal tuberculosis. It is interesting to note

saccular ends, apparently blind, when filled with India ink, demand our closest attention. On the other hand, in some other glomeruli we observe the following. In the pedicle of the afferent and efferent vessels there is, sometimes, a great sinus filled with India ink, from where numerous formations spread creeping to the depths. It may also be observed, in some glomeruli, that the remarkably different sizes of the afferent and efferent arteries vary extremely. There are some glomerular elements in which the efferent artery is half the size or perhaps even less than the diameter of the afferent artery, but, nevertheless there are others in which the afferent and the efferent arteries have practically the same size. In the latter and under these circumstances, we also find those glomerular formations shaped like fingers and like blind evaginations folded upon themselves. No loop-like formation can be categorically proved.

We also find, and this time in pathological kidneys, the following facts. Should it happen that in the observation field the section of the glomerulus had simultaneously contained the afferent and efferent arteries, we would frequently find that these, which are practically of the same size, join within the glomerulus, form the same pedicle and are separated only by a sclerogen connective tissue. This particular formation undoubtedly reminds us of the glomerular afferent arteries in normal cases. If we observe thoroughly an afferent and efferent artery in a normal glomerulus, we shall see that there are two tubes that enter the glomerulus as the barrels of a gun, joined by their walls and separated one from the other by a connective tissue that would seem to belong exclusively to the walls of both vessels. They are joined not as two different tubes being adjacent to each other from the outside of the glomerulus, but as if it were the wall of the vessel enfolded over itself (fig. 1, A, B, C).

However these facts of injection of the kidneys with India Ink prove absolutely nothing, but they incline us to doubt. How could we demonstrate that these evaginations, that we believe to be blind, are not the loops commonly described?

For it, we turn to the technique of injection of the renal parenchyma with plastic elements, be it latex diluted in ammonia or celluloid. Injection with celluloid practiced by a pressure higher than the one the living being has, such as we did in our first experiments, gives us the following results: the arboriform arteries perfectly filled. We can see in some photomicrographs here enclosed and especially in figure 1, D, how an arcuate artery gives off a lobular artery from which several arterioles spring, each arteriole will form a glomerulus perfectly rounded as if they were peas and an afferent and efferent vessel go in and out through the same place. Besides we can observe other formations that will help us to make this clearer. We see in figure 2, 1 an isolated glomerulus in which a plastic substance has been injected by pressure. This glomerulus, rounded in the shape of a pea, has a third tube that no doubt corresponds to the convoluted tubule, that is also filled. How can we interpret this fact? The logical interpretation that we must undoubtedly give it is the following. The pressure with which the plastic substance has been injected has been stronger than the normal pressure, it has caused rupture of the glomerular epithelium and has allowed the

substance shows the shape of Bowman's capsule but not the shape of the glomerular tuft itself

In order to solve the problem, we have used the same injection of plastic substance, but with a much less pressure than the pressure habitual in the living being. We have carefully injected the plastic material with a mercury pressure that does not exceed 10 or 11 cm. To be more didactic, let us begin with the celluloid images. Observing figure 2, *A*, we see the glomerulus absolutely filled, the plastic substance has passed through the glomerular capillary and has spread within Bowman's capsule, establishing another structure, that is seen to the left, and that corresponds to a tubule. The corrosive substance has worked around destroying the organic parts but, precisely here, as Bowman's cavity has been filled, the same pattern remains even if what is organic has been destroyed.

Let us observe figure 2, *B*, also filled with celluloid. Here we see a glomerulus in which this plastic substance has entered the glomerular cavity but has not

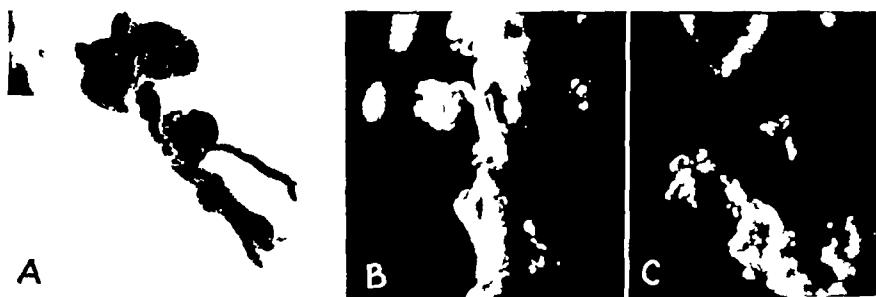


FIG 2 *A*, glomerulus of figure 1, *D*, 4 by 10 objective. Note, besides, initiation of convoluted tubule. False cast because of rupture of capillary sinus. *B*, glomerulus injected with celluloid under controlled pressure. Bowman's capsule has been fully corroded, but interglomerular organic substance has not yet fallen off. *C*, glomerulus injected with celluloid under controlled pressure. Corrosion carried to maximum, very careful washing. Thoroughly observe that there are no loops, but only endothelial evaginations finger shaped and ending in blind saccular arrangements, that join within a great interglomerular sinus. Correct image.

opened its way through the endothelium and, for this reason, it has not spread through the glomerular tuft. The corrosive substance has totally destroyed Bowman's capsule and the tubules, so that we observe a bunch or cluster, so to speak, of elements that do not show a differentiation that might induce us to think that they are loops or other formations. We believe that this happens simply because the corrosive substance has not worked in between the capillary divisions, not permitting a neat differentiation of the individualization of the glomerular elements.

In figure 2, *C*, where the corrosion has been carried more deeply and the subsequent washing has been thoroughly done, we find out something very interesting of which we have previously spoken. In this glomerulus in which the corrosion has been complete, we can see that, instead of a looping system, there occurs cul de sac arrangements. The glomerular elements seem to be shaped as a closed end of a sac that, observed from different angles, can be seen joining at the same spot and that are floating or waving, so to speak, in the surrounding medium,

Unilateral tuberculosis Epididymis Bilateral epididymectomy for a tuberculous process was performed in 36.3 per cent of our cases. This compares with 39.3 per cent in Kretschmer's¹⁸ series, 41.6 per cent in Barney's group,¹⁹ and 63.6 per cent in Hunt's cases.²⁰ In an autopsy series from our institution bilateral involvement was observed in 70 per cent of the cases. The reason for the discrepancy between the clinical and autopsy cases may be explained by the fact that the more advanced processes are bilateral and also that smaller foci may first be discovered after the organ is removed.

The large number of unilateral cases may be explained by the extension of the tuberculosis from caseous tuberculosis of the prostate by way of the ductus deferens.

Complications A comparison of the complications following the operative procedures in genital and renal tuberculosis reveals two interesting findings: 1) that complications following nephrectomy (39.4 per cent) are almost twice as frequent as those after epididymectomy (22.6 per cent) and 2) that slightly more than half the cases in the nephrectomy group were admitted for excision of a post-nephrectomy sinus, whereas less than one-third of the cases of epididymectomy were admitted for excision of the sinus.

The presence of troublesome sinus which developed from a few days to many months after the nephrectomy in 26 per cent of the cases performed at our institution although a frequent complication has been more encouraging than most reports in the literature would seem to indicate (Scholefield²¹ Crabtree and Cabot²²).

Scholefield²¹ believes that the development of a sinus is not due to the continuation of any existing infection but rather to the development of new tuberculosis in traumatized tissue of a patient with lowered resistance. The lower resistance of the patient is the most important factor. We find it difficult to accept this point of view since the new tuberculous process necessary to form the sinus tract would necessitate a hematogenous dissemination to the soft tissues in this area. Hematogenous seedings to soft tissues are rare indeed, while a sinus tract following nephrectomy is common.

Hale²³ who reports a 17 per cent breakdown of the wound before discharge attributed his good results to removing as much of the ureter as possible through the usual incision and injecting the lumen of the ureter with phenol.

The treatment of sinus tracts has today almost become academic since the introduction of dihydro-streptomycin in the treatment of tuberculosis. All studies have shown that this drug shows its greatest efficacy in the closure of tuberculous sinus tracts.

Cost of death We are aware of the fact that some of the patients who were lost to our study may have died as a result of the disease. We believe that this number would be small because most of these patients are those with the tuberculous disease arrested.

¹⁸ Kretschmer H. I. Surg. Gynec. & Obst., 47: 652-659, 1928.

¹⁹ Barney. Quoted by Kretschmer.

²⁰ Hunt V. C. Arch. Surg., 8: 811-818, 1924.

²¹ Scholefield B. G. J. Urol., 20: 345-353, 1928.

²² Crabtree I. G. and Cabot H. Surg. Gynec. & Obst., 21: 669-679, 1915.

²³ Hale N. G. Trans. West. Sect. Am. J. Urol. Assoc., 5: 21-24, 1930.

correctly performed, they would not be sufficiently categorical if we do not complete them by transmitted light. In figures 5 and 6 we have the same glomerular image but viewed by direct and transmitted light. We see, for instance in figure 5, *A*, that the pattern formed by the latex, that fills absolutely the glomerular tuft, has several characteristics. Some glomeruli look massed up and undifferentiated, in others, instead, the corrosion has worked deeply and has been able, as shown in this preparation, to dissect all the elements of the tuft, that are blind ending saccular formations, coiled upon themselves and intertwined with the neighboring ones. We also see, in another glomerulus (lower part) an afferent and efferent vessel, practically of the same size, that goes in and out through the same place. In this photomicrography, the glomeruli to the left are especially interesting, in them, we can perfectly see some formations having the shape of blind ending saccular outgrowths, as if they were sea anemones with open tentacles. This same preparation viewed by transmitted light (fig. 5, *B*) completes



FIG. 4. Glomeruli injected with latex. Fully performed corrosion. Capillary formations end individually and in blind saccular arrangements.

the preceding image. Let us observe in the group of three glomeruli, that the corrosion, though quite deep, has not been perfect, leaving some protoplasmatic cellular elements of Bowman's capsule that enfold the glomerulus. There undoubtedly lies the error of former investigators, that have not obtained total elimination of the protoplasmatic elements. While in the group of glomeruli to the left, the corrosion has worked deeply and we may observe, through transparency, as if it were in a Chinese image, how the glomerulus is formed by dendritic evaginations, instead of being formed by loops. We complete the image with the figure 6. It is a preparation of a pathological kidney, in which most of the evaginations are atrophied and in which the capsule and the proximal convoluted tubule are visible because of lack of complete corrosion and of a loosening of protoplasmatic substances. It can very clearly be seen how, in contact with the afferent artery there is a zone like a sinus, from which several evaginations radiate all ending in blind tubule arrangements and none of them in the shape of loops. In this glomerulus all other evaginations have probably disappeared due to

renal tuberculosis should not be operated upon. The remaining 9 instances were those in which the renal tuberculosis in the opposite kidney developed from 9 months to 10 years after nephrectomy.

The cases of uremia in the series of genital tuberculosis include 6 of the cases in which both a nephrectomy and epididymectomy were performed. There were 3 cases in addition in which extensive bilateral renal tuberculosis also existed in which no surgery on the kidney was attempted.

Death due to tuberculous meningitis was a more frequent complication of genital (11.6 per cent) than renal tuberculosis (4.2 per cent). The two nephrectomy cases of this group also had an epididymectomy. Kretschmer¹⁸ found tuberculous meningitis as the most frequent cause of death in his series of cases of genital tuberculosis.

The question has often been raised as to whether tuberculous meningitis is a complication of the operative procedure. Turner²⁶ felt that there must be a factor in the operation itself which encourages the dissemination of the bacilli and he suggests rude handling with contusion of the tissues and soiling of the fresh wound by pus from renal abscesses containing bacilli.

Our own experience is that tuberculous meningitis in adults is part of a generalized military tuberculosis (usually secondary to active skeletal or urogenital tuberculosis) and occurs more frequently in nonsurgical than in surgical cases.

Amyloid uremia secondary to an extensive amyloid deposition in the glomeruli of the kidney caused the death of the patients in 8.4 per cent of the nephrectomy cases and 6.8 per cent of the epididymectomy cases.

SUMMARY

An 18 year follow-up study has been presented on 209 cases operated on for renal and epididymal tuberculosis. An epididymectomy was done in 105 cases, a nephrectomy in 63 and in 41 both an epididymectomy and nephrectomy were done.

Chronic pulmonary tuberculosis was also present in 50.0 per cent of the nephrectomy and 70.6 per cent of the epididymectomy cases, associated bone tuberculosis occurred in 23.1 per cent of the patients with renal tuberculosis and in 24.6 per cent of the cases with genital tuberculosis.

Postoperative sinuses developed in 38.4 per cent of the nephrectomy series and 22.6 per cent of the epididymectomy series.

There are 49.9 per cent known deaths in this series. The chief cause of death in both the nephrectomy and epididymectomy patients is chronic pulmonary tuberculosis. Uremia is a more frequent cause of death following nephrectomy while tuberculous meningitis is a more frequent occurrence after epididymectomy.

We are indebted to Dr Philip Baron, resident in urology, and Miss M. Norton, record librarian, for their valuable assistance.

are other dendritic evaginations enclosed within Bowman's capsule still not fully corroded or removed. It is useless to add more illustrations, we have numberless, obtained from these preparations, and they all agree in the same fact.

The glomerulus appears in digitated arrangements and never in looping formations. The afferent and efferent vessels passing through the same place and always joining in the same cavity.

When the glomerulus is atrophied, the afferent and efferent vessels form practically one, and there lies, once again, the proof of the origin of Ludwig's "vasa recta vera." According to these findings, our conception of the glomerular image is totally different to Wimtrup's conception and resembles still less the arteriolar massing up accepted by former authors. For us, the glomerulus is formed by the evagination of an arteriole, an evagination that shapes itself in a multiple formation, each determining saccular blind ending outgrowths. Their object is to increase the filtration surface in a limited space (fig 7, 4). The more

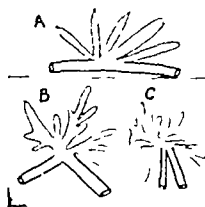


FIG 7 4, glomerulus vascular portion is formed by evaginations of a single vessel and not by two vessels joined by a looping system. B and C, single vessel bends and is crowned by blind ending dendritic arrangements, which secure an increase of surface for ultrafiltration of blood.

elements of this sort there are, the wider the filtration surface will be, and each of these evaginations in their turn, may produce other evaginations so that the filtrate quantity be increased.

The afferent and efferent vessels stop being two vessels, so to speak, to become only one. This vessel will adapt itself morphologically to the future glomerular function, and will bend in the same place from where this endothelial evagination branches off, so that the afferent artery may, in contact with the efferent, form a gun barrel. All this dendritic endothelial evagination will richly expand precisely in the bend of the vessel. The dendritic endothelial evagination will gather all around the bend of the artery. Hence the glomerular characteristic that we usually see (fig 7, B and C) a tuft that crowns an afferent and an efferent vessel. For us, these afferent and efferent vessels are only one vessel crowned with dendritic evaginations, that will form the tuft. The object of this tuft being the ultrafiltration of the blood and the formation of the first urinary stage.

Even if this conception agrees with the anatomical findings that the corrosion patterns and photomicrographs show, they must be fully confirmed. We may have the need of changing our conception through other evidences, but to make the investigation true and more systematic, we have decided to perform sections in series. If we saw that these afferent and efferent vessels joined in a certain place forming a common sinus, we should have practically demonstrated the indivisibility of the vessel. For it we have performed sections in series and we have

ing his hands, even though a surgical cap is being worn. Although the surface is not a true optical surface, experience has not shown enough distortion to be of significance. The plastic surface is comparatively soft, so that eventually the eyepiece of the cystoscope will cause scratch marks. As soon as these become troublesome, the plastic eyepiece can be quickly and cheaply replaced. They can be sterilized only in cold water solutions, such as the mercury compound solutions at present used for cystoscopes. The goggles are inexpensive, costing only about \$1.25 each, so that several pairs can be kept on hand and new ones slipped on for each case. They are open above and below, and so there is little tendency to fog. They have proved to be comfortable. We believe the use of these or a similar type of goggle will greatly reduce the incidence of contamination of cystoscopic instruments.

These goggles are made by the Chicago Eye Shield Co., 2300 W. Warren Ave., Chicago, Ill., and will be obtainable from V. Mueller & Co., Chicago

1819 W. Poll, Chicago 12, Ill.

MEETING OF NEW YORK SOCIETY AMERICAN UROLOGICAL ASSOCIATION

February 27, 1952

Yale Club, New York, N. Y.

8:30 P.M. PAPER OF THE EVENING

Dr. Elmer Hess, President, American Urological Association, Erie, Pa.

Renal Ptosis

Discussion: Dr. Austin I. Dodson, Richmond, Va.,

Dr. George W. Fish, New York, N. Y.

by mesenchymatous elements from the renal blastema and that will immediately change into an empty hollow tube that will surround practically the whole surface of this sanguineous lacuna issuing from the capillary. This element is of great importance for our conception of the glomerulus. Let us see now the evolution of this glomerulus, following our preparations.

If in the embryo we meet the first evagination stages of the vessel and of the glomerular sanguineous lacuna, we could say that embryology agrees with us.

If we observe an embryo kidney with the microscope and, to be more exact, a metanephric kidney, we shall be able to observe in it all the evolutive stages of the glomerular lacuna formation, from its origin to its definite establishment, in an anfractous and unrecognizable form, such as we have found in the adult. We know that in the metanephric kidney there are different evolution zones of the nephron. The most central zone and the one closest to the medulla contains practically normal glomeruli under certain circumstances and when the organ has further developed. But, as we leave the central zone and go towards the periphric zone, we find all the stages of glomerular evolution to the most primitive.

Let us see now how a glomerulus develops. According to the following photomicrographs we observe that, in the peripheral zone, the renal blastema gives off some convoluted tubular formations in zig-zag or S-shaped and many times snail-like, that have many special characteristics (fig 9, A). In the edge of this tubular formation there is a small sanguineous lacuna which, we shall see if we observe, will form a capillary. That small sanguineous lacuna in contact with the wall of the tubule tells us that it is the formation of a glomerulus, since the opposite wall of the tubule loses its characteristic mesenchymatous cell fence to transform itself to endothelium. The lumen of the cavity of this capsule, interposed between this wall and the one placed against the glomerulus, will continue in the pre-established tubule. The small sanguineous lacuna, an evident dilatation within the capillary system, that is developing within the embryonic kidney, will proliferate, will grow, will turn crescent shaped sometimes and rounded others, that is to say, we shall see a sanguineous sinus with an entrance and an exit, filled with red blood cells (fig 9, B). This sinus, in the shape of a vessel evagination, is surrounded by a cell fence that will form, later on, the glomerular endothelium of Bowman's capsule. If we follow the observation in the same kidney, a little deeper, we shall see, under certain circumstances, in this same sanguineous lacuna that we are describing, a very special characteristic: evaginations and furrows produce themselves on its surface, evaginations that reach sometimes even the lumen of the vessel. These evaginations will produce themselves in several forms, they will begin by one, two, three and so on, giving successively the glomerulus the bifoliate, trifoliate and multifoliate aspect (fig 9, C). In this observation we can appreciate that an single vessel practically straight in a certain moment, has produced an endothelial evagination and starts producing the invagination of the same endothelium, to enlarge the filtration surface of the glomerulus. We also observe another strange fact. The sanguineous sinus that has divided itself in several sections, but always attached to the same vessel in the lower zone, assumes a rounded shape. The same vessel

STRUCTURE OF THE GLOMERULAR TUFT

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When in 1866 Malpighi discovered his famous glomeruli, he supposed they were composed of arterial elements massed upon themselves and that they had as their principal function the physiological need of urinary formation. Ever since it has been supposed that glomeruli consisted of arterial capillaries but, though this supposition is exact, a complete record has not been reached on how this formation was distributed. In 1928 Vimtrup described it as elements that form loops joining two vessels, an afferent and an efferent one, the afferent vessel is of a larger size and the efferent of a smaller. Ever since no more investigations have been practiced to determine if these loop-like formations are absolutely true or if there could not possibly be any other anatomical manifestations, that could change this concept. According to Vimtrup, as we have said the afferent artery branches dichotomously or not into several other vessels that in their turn, join themselves at the other end, forming another artery that provides egress to the contents. That is to say the arterial blood flowing in through the afferent artery distributes itself through many capillary loops, that may be from eight, twelve to eighteen, according to some authors, and that converge before ending into another artery of much less caliber than that through which it has flowed in. This conception of Vimtrup, accepted by all the anatomists and even by the physiologists, does not of course satisfy entirely especially if we think of the function of the glomerulus, normal as well as pathological. So much so that, in order to explain some pathological facts, other investigators have adapted some modifications to the glomerulus such as Gormaghtigh's, 1938, where he tries to explain the isolation of the tuft and the continuity of the blood to the small efferent artery, by means of a special arrangement that changes the course of this blood directly without the need of passing through the glomerulus itself.

Considering it physiologically, the glomerulus is a filter that lets the water and electrolytes pass, retaining within its tuft all the elements that have molecular weight superior to 30 000, that is to say that, an intense concentration of plasma occurs at a certain moment, with a remarkable use of the viscosity of the blood.

There exist approximately a million glomeruli in each kidney, their physiological work is normally reduced, in ordinary life, to approximately a third part of them. Besides with the actual conception of the glomerular structure, the efferent artery, that has its origin in a non-intercommunicated network of many branches ends in a capillary group that surrounds the tubules whose object is to gather the filtered elements that must be re-absorbed by the blood, to be given back to the general circulation. Now then as we have said, it is difficult to imagine or at least to explain logically how if two thirds of the glomeruli of the kidney must rest this partial circulation can be interrupted, be it only for a short

the production and activity of the metanephros. So, since the establishment of the first glomerulus till the moment when the kidney stops functioning, new formations are constantly being produced. In a 17 days old rabbit embryo we will see, in the lower part of the wolffian body, the developing glomerular formations where, among the tubules, a small sanguineous lacuna develops—as may be observed especially in one of the illustrations (fig 9, *D*). If we observe this preparation and the preparations of the former and latter sections, we shall see that the small sanguineous lacuna has a relation with the rest of the circulation by means of two small entrance and exit zones, that join all the circulating elements that are in the mesonephros. This small sanguineous lacuna, with an entrance and an exit mouth, assumes a shape of a crescent and is surrounded only on one side by a fence of cells that belongs to a mesonephric tubule that has its origin in the mesenchyme of the wolffian body. This small sanguineous lacuna will suffer a perfect determined evolution. Precisely beside it we observe a more differentiated evolutive stage and we can see how this sanguineous lacuna has divided itself practically in two. It also has a zone of entrance and another of exit that belong to the same vessel. Thus, if we observe all the other elements that exist in the mesonephros, we can perfectly distinguish series of glomeruli in which the lacunar formation has a shape of a rounded crescent, without evaginations, others have series of evaginations and invaginations that will transform this lacuna in an irrigation zone of foliated aspect, having one, two or more sections. These evaginations acquire special characteristics, sometimes these arrangements are enfolded endings, wide spreading, but always filled with blood, and all of them joining in a small vascular pedicle, where the afferent and efferent vessels can be seen. The same thing happens in the mesonephros as in the metanephros, but in a more primitive form, not only by its formation period—which logically happens before in the mesonephros—but also more primitive in the anatomical characteristics. The evolution of the glomerulus and specially of its sanguineous lacuna is more evident because it happens in a more simple form. The quantity of cells, that seem too numerous considering the total size of the embryo, is evidently less than that in the metanephros. That is why the mesonephric demonstration is as important to be proved as the metanephric.

DISCUSSION

As an exordium we have expressed our doubts as regards the glomerulus formation such as Antrup described it in 1928, and such as it has been discussed since Malpighi. We believe now that if we consider the glomerulus as an evagination of a single vessel spreading in branches—in order to increase the irrigation surface—we can perfectly explain some physiological facts that have aroused our doubt. But first of all we must think how, if there is no network interposed between an afferent and an efferent vessel, can the urine possibly filter?

We believe that the conclusion is simple and perfectly logical, and that the organism has adapted that function to the vessel that gives birth to the evaginations.

have, causing an evident circulatory delay, which is practically impossible either to demonstrate or to see

Histologically, the efferent vessel is formed exactly in the same way as all the other vessels and arterial elements of the kidney

These objections of physiological origin are, besides, reinforced by what is observed in renal disease, where a great quantity of elements and facts are very difficult to interpret, if we consider the renal glomerulus according to the accepted general conception. In the renal ischemia cases, for instance, once the ischemia has been established by vessel constriction, if the blood should really flow through the glomerulus we would gather a quantity of facts of great importance. In these cases the urine is not being produced or, at least, the physiological function of urinary elaboration is deeply altered, nevertheless, the blood passes through the kidney, flows in through the renal artery and along the vein practically at the same rate and in the same quantity as the blood that passes through the artery. That is to say, the renal circulation does not stop. The only one interrupted is the glomerular circulation. How can this possibly happen if every renal artery must necessarily branch off and its arteriolar branches must also necessarily pass through a glomerulus? The few arteries that end without glomerular interposition are only the capsular arteries. Later on we shall discuss the constitution of the *vasa recta vera*. It is difficult to imagine that, when renal ischemia occurs, the kidney stops functioning. If blood flows in through the artery and along the vein, it should necessarily pass through the glomerulus according to the modern conception, nevertheless no urine is being produced or, is it that the blood does not perhaps pass through the glomerulus?

On the other side, when we observe chronic glomerulonephritis, we can see in the glomerulus certain extremely interesting anatomopathological facts. Before sclerosis of the glomerulus occurs and its total transformation into a hyaline mass, a great vascular sinus produces itself in the pedicle and in intimate relation with it. This sinus should seem to deviate the blood from the afferent arterial branch directly to the efferent arterial branch, excluding the glomerulus that becomes then easily sclerosed, because of an intense reaction of its histiocyte elements. Naturally, we do not want to go into details of the histogenesis of the facts because they would take us too long and this is not our purpose.

Another pathological fact that is also difficult to explain with the present conception of the glomeruli is glomerular hydrops. Once a glomerular hydrops is established, it should, because of the pressure that the liquid establishes in Bowman's capsule, stop the glomerular circulation and cause, then, ischemia of the efferent vessel, a thing that does not happen. We may see, in hydropic state, a glomerulus made small and emptied of blood, but we see an efferent artery that contains blood and that irrigates the corresponding tubules and helps to diminish the repletion so to speak of such glomerulus, absorbing liquid and absorbing the elements that must be restored to the blood.

Another fact of pathological anatomy in the already advanced glomerulonephritic states is the degenerative glomerular process of Trueta and the *artery formation (vasa recta vera)* of Ludwig. Ludwig's *vasa recta vera*, considered by

diminish considerably in its afferent and efferent portions, diminishing also the flowing of the blood into the glomerular zone. But another phenomenon may happen, this is the dilatation of the efferent vessel, that practically reaches the same size as the afferent vessel, such as we have already observed. Trueta had settled this perfectly in his works, and Claude Bernard also conjectured it a long time before then.

The dilatation of the efferent vessel, produced by sympathetic or parasympathetic phenomena, not yet well determined, will allow the sanguineous stream to flow from the ingoing vessel directly out to the theoretically outgoing one, that is to say, the glomerular vessel that we described will acquire the same caliber in the afferent and efferent glomerular portions. Then the stream will pass directly, flowing into the portal arterial renal system and ending within the venous vessels to flow into the general circulation, totally excluding the glomerular zone. This conception is absolutely unacceptable if a looping system should exist between an afferent and an efferent vessel. This physiopathological fact demonstrates that the glomerular vessel is only one and that it is not divided and has no looping interposition between one and the other.

We can also explain how, physiologically, the two thirds of the glomeruli rest while a third of them works. With the interposition of a looping system between one vessel and the other, we could not think of a glomerular rest, the blood would be flowing constantly through this vascular system. But should there be a single vessel with dilatations and evaginations exclusively on one side, the rest of the glomeruli would be easily explained. There is no need for the glomerular sanguineous lacuna to be constantly full, if through sympathetic regulation the efferent vessel widens, the blood will flow directly from the afferent to the efferent glomerular zone, that is to say, directly through the vessel with no need of filling the vascular lacuna. With it we shall not only have the glomerulus at rest, but we shall also have the evacuation of the sanguineous elements that are within the glomerulus, that is to say, the figured elements and all the molecules of a bigger size than the albumin molecules. All those molecules that would not pass through the glomerular ultrafilter, at rest, would be swept away and absorbed by the stream to be given back to the general circulation.

On the other side, with our conception of the glomerular circulation, we can explain how the blood, deprived of the electrolytes and of the plasma elements which are smaller than the albumin molecules, does not suffer such a great hematic concentration as to be able to alter the glomerular circulation, establishing a circulatory delay by increase of viscosity. It is not absolutely necessary that all the elements should pass straight through the glomerulus to form the urine, it is perfectly possible that the blood, filling the glomerular lacuna and because of its excessive affluence within the glomerulus, will flow directly through the efferent portion of the vessel with no need of producing an hemoconcentration of such a character that might hinder the course of the blood and would pathologically alter the efferent vessel and the portal arterial system. This would alter its functions and its anatomical integrity.

This cannot be conceived in any other way if we believe that there is a network

entrance and exit of the vessels. As regards the introduction of strange elements in the kidney and in order to prove this experiment to be true, we have always employed the following method of preparation. A kidney surgically removed, either pathological kidneys from patients of the hospital or removed immediately after a death produced by other causes or from animals put under ether anesthesia, we submitted these kidneys to a careful washing, but under controlled pressure. For it we use a manometer common in physiology, that consists of two U-branches, one contains water and the other contains mercury. They are intermittently joined by a Richardson's insufflator and a bottle where the liquid to be injected into the kidney is placed. From there comes out a tube that joins another T-tube, connecting the bottle to the manometer. Then we proceed to wash the kidney. The washing is done simply with water and with a pressure that is never higher than 10 cm. mercury. So as to be more careful we generally use the water column, being much more sensitive as regards pressure increases. Water is introduced through the renal artery and the washing is not interrupted till the water comes out absolutely clean through the renal vein. Once this obtained we proceed to press the kidney slightly to eliminate the liquid left. Then we change the liquid to be injected by a very fluid celluloid solution in acetone, in the first group, and by another of latex diluted in ammonia in the second group. When the kidney is injected with India ink or with plastic substances of hardening or moulding we plunge it into a 10 per cent solution of formol for its due fixation and hardening. If the kidney is meant for the microscopic anatomic study, we follow the different stages of the pathological anatomy and histology preparations. In these cases we use the kidneys injected with India ink in serial or in single sections, while in the kidney in which plastic materials have been used, to show its arterial and glomerular structure we corrode every organic substance with hydrochloric acid, one part in two of water and then we submit it to a careful washing compressed under a slight water pressure in order not to destroy the very delicate glomerular formations.

RESULTS

In the first step when we have studied the glomerulus injected with India ink and in single sections we already observe some very interesting manifestations that we should like to follow with the present photomicrographs. We have observed the following: filling up a kidney with India ink we can see that not all the glomeruli are filled with India ink but only a limited group that could be a third of them or maybe a little more. In them we can observe the afferent and the efferent glomerular arteries filled with a substance that makes the elements visible and we also see the complex glomerular tuft formed by outgrowths that seem to be digitated such as the finger ends of a glove. Some of them are branched, others simple and most of them coiled upon themselves in capricious shapes such as S-shapes or sharp curves so that they look like a mass of articles of a sea anemone, folded upon themselves but to all appearances *unlike* one from the others. Up to now we could agree with the idea of the loop formations but we must undoubtedly acknowledge that these glomerular

dropsy would produce itself caused by nephrosis of the lower nephron or by any type of nephrosis or nephritis. This is due to the constitution of the glomerulus in an only vessel and a sanguineous lacuna through evagination, and to the blood flowing easily from the vessel called afferent to the vessel called efferent, without interposition of a network system. The evagination we speak of, is left aside from the sanguineous stream through the vaso-dilatation of the efferent zone of the glomerular vessel. Simkin and associates, to demonstrate the diverting of the blood through the juxtamedullary zone, carried out an experiment that consisted of injecting small glass spherules through the renal artery and they found that these spherules came out through the renal vein, well then, if in the glomerulus there were a capillary looping system, the spherules diameter being 400 microns, they would never pass through the glomerulus. That is why there must be another mechanism that permits these spherules to get back through the renal vein, and this mechanism is simply the anatomical conception we propose: a sphere of a size that would go in through the renal artery and would go out through the vein, would have to pass directly through a vessel of a caliber of the glomerular vessel, it would have to pass through a single vessel that keeps, in a certain moment, the same diameter in the going in and the going out portions: these spheres have then no reason to go into the sanguineous glomerular lacuna, and they pass straight—aside from the glomerulus—through the same afferent and efferent vessel and from there to the renal vein.

This experiment by Simkin and his associates was conceived in order to explain Trueta's "short-circuit" and the juxtamedullary glomerular circulation of the kidney, it is an experiment that also categorically explains the conception we propose of the glomerular circulation.

As regards the pathological phenomena that take place in the glomerulus by marked alterative processes, it is easy to conceive the following facts: we have observed that, as the glomerulus scleroses, an exterior sanguineous lacuna establishes itself, changing later on into an uninterrupted cavity between the afferent and efferent vessel, so much so in these circumstances that this vessel acquires a characteristic of a single vessel, this would be called, in anatomy, Ludwig's "vasa recta vera", and it is a pathological demonstration of the conception we propose of the glomerular circulation. This is simply due to the fact taking place in a same and single vessel and that the evaginations that contributed to the renal filtration, due to infection and to pathological alterations of the glomerulus, disappear and change into hyaline substance. But the sanguineous stream flows on without suffering any change, from the afferent to the efferent portions of the vessel to join the general circulation through the venous channels. There are some images obtained in plastic material, in Trueta's work, that categorically demonstrate the formation of the "vasa recta vera" at the expense of the glomerulus sclerosis. We imagine how difficult it should be, if a looping system existed between the afferent and the efferent vessel, to work a cavity within a hyaline tissue, that would carry the blood from one vessel to the other, we think that if this hyaline tissue that, in the former conception of

passing of the plastic substance to Bowman's capsule, that has been totally filled in a rounded shape, besides, plastic substance has passed to the convoluted proximal tubule. We can then say that these rounded glomeruli, described in

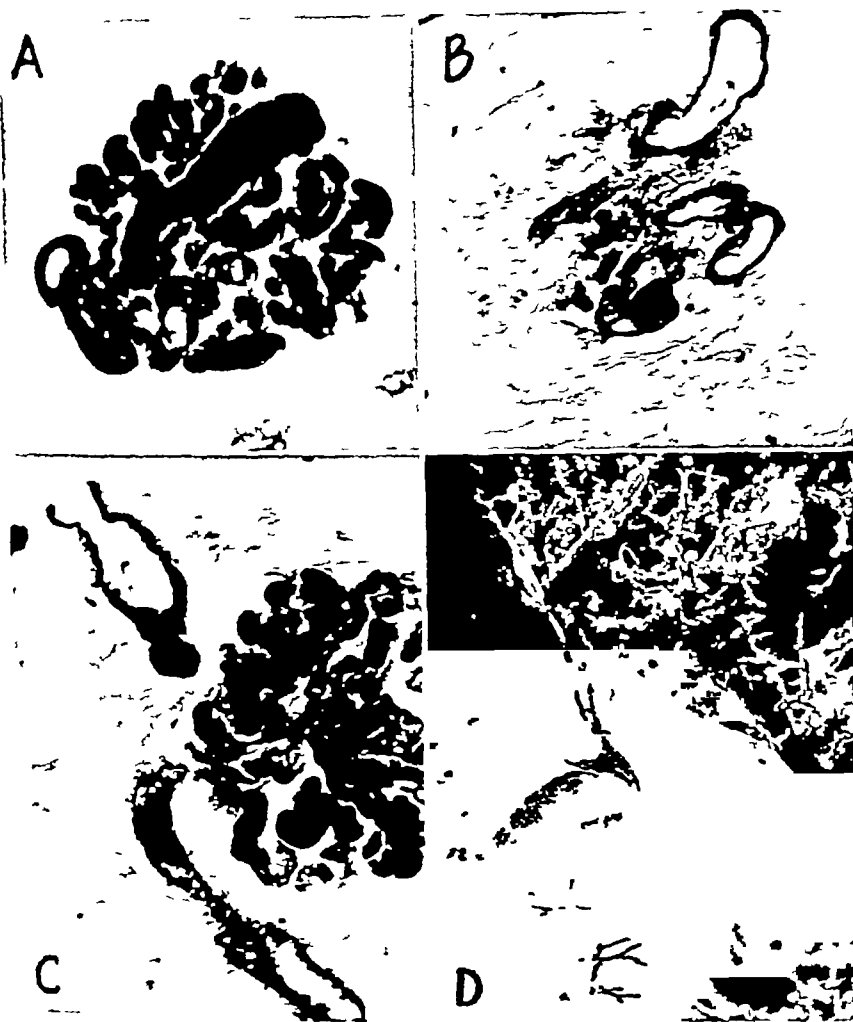


FIG. 1. A India ink injection, 4 by 10 Leitz objective. Glomerular blood sinus with afferent and efferent vessel joining in it. Capillary formations seem to end in saccular arrangements. B India ink injection, 4 by 10 Leitz objective. Glomerular vessels seen when entering tuft. Twisted and coiled up capillaries, but apparently blind ending. C injection with India ink. 4 by 10 Leitz objective. Glomerulus with degenerative process of hyalinization. Afferent and efferent vessels of same caliber, their walls being in close contact. D, celluloid mould. 2 by 10 Leitz objective. Note artery from where an interlobular arteriole shoots off and from it countless per like glomeruli. False view due to excessive pressure that compressed plastic substance, which filled Bowman's capsule because of rupture of capillary sinus.

Our glomerular investigation work, are probably due to the plastic substance injected in Bowman's capsule and are not, then, a faithful reflection of the arterial system of the glomerulus but an artificial one caused by an injection of too strong pressure that has determined the rupture of the tuft. Truly, the plastic

AN IMPROVED INSTRUMENT FOR LAVAGE OF THE OPENED RENAL PELVIS

RALPH B MULLENIX AND ROBERT J PRENTISS

The need for a simple and efficient device for the thorough lavage of the opened renal pelvis is well known. Dislodgment of tiny calculi, fragments of calculi, clots, etc., occasionally offer real difficulty. Evacuators and similar instruments previously devised have been deficient in many respects and most operators eventually have become dependent upon forceful flushing of the kidney pelvis with a small catheter or tube powered by whatever type of syringe could be found on short notice at the operating table.

The authors have developed a highly satisfactory apparatus which is effective and dependable. This apparatus was exhibited in the new instrument section of

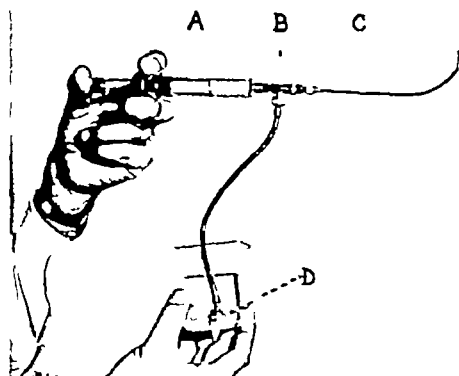


FIG 1

scientific exhibits at the Western Section of the American Urological Association in the Yosemite Valley in May 1950. It consists of an assembly of standard items of readily available and inexpensive equipment which can be kept in constant readiness in the surgeon's kit or in the surgical instrument room.

The individual items used in the assembly of this apparatus are illustrated in figure 1. They are (A) the Yale B-D Lok-Syringe with finger rings (Becton-Dickinson No 10 YLC), (B) the automatic double valve with B-D Lok-Syringe connection (Becton-Dickinson No 470V), and (C) the malleable laryngeal cannula (Becton-Dickinson No 456).

After the component parts have been assembled, the weighted intake tube (D) is placed in a container of water or saline which is held by the nurse, and the surgeon is then able by rapid manipulation of the syringe to propel an almost continuous jet of solution into the kidney pelvis. The self-filling type of syringe makes it unnecessary to engage in repeated disconnections and refilling operations, which are always disconcerting and time consuming. The malleability of the cannula makes possible any adaptation to the shape of the renal pelvis and the cannula tip can be introduced successively into any and

but each of them individually We have not observed loop-formations, as described by Wimtrup, in any other preparation similar to this one

We found some objections to the celluloid images since they present elements of such fragility that the slightest movement or striking caused the immediate loosening of the glomeruli, we had to correct these errors of technique with the latex injection The latex injections have offered us anatomical findings that complete, and absolutely verify what we have observed in the celluloid preparations Let us follow the preparations with the photomicrographs as we did before In figure 3, two great interlobular vessels can be seen, with glomeruli attached to them by means of their respective capillaries In them the glomerular tuft is massed up and indistinguishable, in the anatomic sense Let us observe how, in some, a large vessel goes in and a small one comes out, in others, instead of a large and a small vessel it is only a big one that shoots off a branch of the same caliber as the parent trunk But, undoubtedly, the corrosive substance has



FIG 3 Glomeruli injected with latex Corrosion has acted differently allowing confusion

has not acted sufficiently so as to differentiate correctly all the elements that compose the tufts except in the one shown in the right upper part In this tuft we may already slightly appreciate the dissection obtained by a corrosion In figure 4 we can see a glomerular arteriole in which the corrosion has been correctly performed We can observe how the glomerular bundle *ends in saccular cylindrical* tube arrangements which are massed up on themselves instead of being closed saccular formations or better said formations communicating through their ends to the afferent and efferent arterioles We observe in the glomerulus edge the saccular blind ends that sometimes branch off but are never anastomosed In this saccular arrangement, apparently blind may have beside it other formations of the same kind also blind that communicate with the same cavity and never with other

Then if we have obtained these conclusive images viewed by direct light in celluloid preparations especially in those in which the corrosion has been

PYOGENIC (FOAM CELL) GRANULOMA IN A CASE OF PYONEPHROSIS

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The case to be reported is such an unusual manifestation of renal disease, that it prompted the authors to make a thorough search of the literature for similar cases. As far as could be determined from the literature available, a report by Barrie (1949) gave the only detailed description of this interesting phenomenon. He referred to two previously published German reports and described two additional cases, in which foam-cell granulomatous nodules were present in the kidney and were mistaken for caseous tuberculosis. One of the German authors (Putschar—1934) described "a vascular granulation tissue, sometimes so rich in foam cells, that it looked butter yellow."

"Foam" cells or lipid-rich cells may be found in a variety of kidney lesions. The kidney normally has a high lipid content and shows a poor fibrous reaction to tissue trauma. Barrie suggested that these cells were derived from fibroblasts at the site of small areas of suppuration. These foam cells may form nodules of varying size or invade the perinephric tissue. The pathological changes may be mistaken in the gross for tuberculous granulation tissue or a renal papillary tumor.

CASE REPORT

Miss L. M., a 35 year old white woman, was admitted on July 13, 1949, to the urological service of the Victoria General Hospital, with complaints of burning on urination, hematuria, painful lump in the right side and recurrent chills. She stated that 3 weeks prior to admission, she began to have "sharp burning" on voiding. The day following the onset of this symptom, she had a small amount of hematuria with severe pain in the right flank. This was accompanied by intermittent "chills." She had no frequency or nocturia. She had been hospitalized elsewhere and treated with penicillin, streptomycin and blood transfusion. Because of a lack of response to treatment and the severity of her illness, she was then referred to our hospital. The family history revealed only that her mother had died of carcinoma of the liver. Her past history was negative except for a "lump in the side," and "kidney trouble" as a small girl. Nothing further could be elicited concerning the latter.

Examination revealed a pallid woman who appeared to be acutely ill. The pulse was rapid but regular, the blood pressure was 135/80, and the temperature 98.6 F. The right upper quadrant of the abdomen contained a firm, smooth, and movable mass extending 3 to 4 finger breadths below the costal margin and to the midline medially. Urinalysis showed a trace of albumin and in occasional pus cells. Her hemoglobin was 70 per cent, and the white blood cells 6200. The nonprotein nitrogen was 20 mg. An excretory urogram showed normal outline and function on the left side, but no dye was seen on the right side.



FIG. 5. 4, glomeruli injected with latex. B, former view taken with transmitted lighting

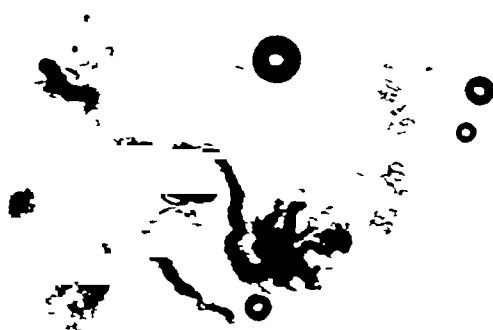


FIG. 6. Latex injection. Corrosion performed in pathological glomerulus. Bowman's capsule and convoluted proximal tubule. Within capsule we see glomerular capillary that through a blood sinus receives endothelial exaginations left.

the sclerosis where only a few elements last that still secure the glomerular organization. Further below there is another glomerulus though not so clearly distinguishable among the other neighboring elements that presents an afferent and an efferent vessel forming only a straight one, and under which there

Pathological description (Dr. J. H. Fodden, of the Pathological Institute): "The specimen is an enlarged kidney, almost totally replaced by a large hydronephrotic sac. There is a hemorrhagic, yellowish-red mass in the region of the upper pole, extending out into the perirenal fat in a polypoid fashion. Microscopically, the characters of this tissue are those of a pyogenic granuloma of the renal cortex and perirenal tissues. Small abscesses can be seen within it, each with surrounding masses of foam cells (fig. 2, A). There is no evidence of malignancy or of tuberculosis."

The postoperative course was stormy. Repeated blood transfusions, gastric suction, intravenous fluids, etc. were all used. The packing was gradually short-

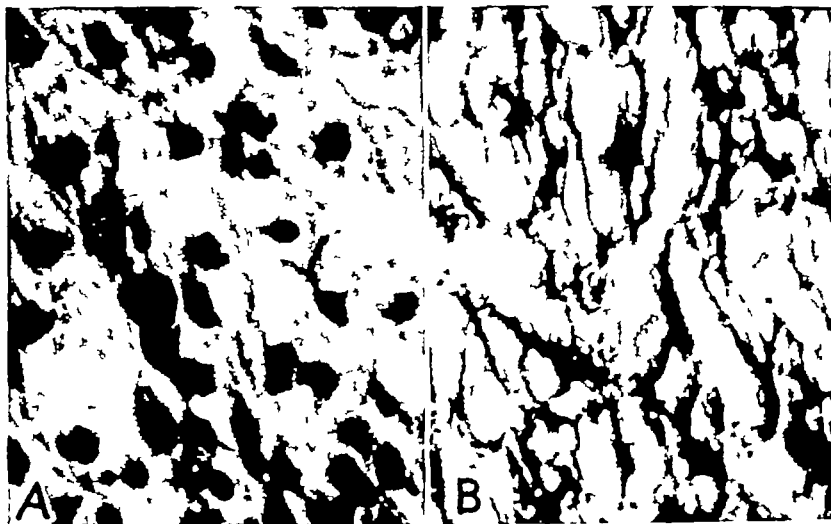


FIG. 2. A, pyogenic granulation tissue shows lipid rich "foam cells" $\times 44$. B, infiltrating granulation tissue shows dense reticulum formation. Wilder's reticulum stain $\times 44$.

ened and completely out by July 29, nine days postoperatively. The patient showed a slow but gradual improvement and by August 19 was gaining weight, feeling well, and was up and about. The incision was well healed except for a slight opening at the upper end. She was discharged to the care of her own physician.

Re-examination on November 21, 1949, showed an apparently healthy woman who had gained weight, had a good appetite and was symptom free. The sinus opening was still present, but practically no discharge was seen. Culture of material from the sinus showed growth of *B. coli*. It was believed that this would close and she was discharged.

A recent communication from her physician in reply to a follow-up inquiry revealed some interesting information. He stated that he had found hydronephrosis on the right side in this woman in 1935, at which time the urine had been reported positive for tubercle bacilli. A recheck in 1943 revealed the same hydronephrosis, but urine studies for tuberculosis were negative. As for her present condition, she was feeling well and the sinus had apparently closed.

been able, in countless occasions, to follow the vessel called afferent and to see how it joins the efferent vessel within the glomerular sinus (fig 8) These images prove this fact categorically

We undoubtedly consider this finding difficult to obtain in the normal glomeruli Both branches of the same vessel penetrate deeply within the glomerular sinus, and the prosecution of the lumen or of the contents of this vessel up to the junction of both branches is difficult, because of the interposition of the filling substances, such as India ink that might arouse confusion This becomes simpler with damaged glomeruli In such cases, when sclerosis begins, the reconstruction of the vessel can be practiced with absolute certainty We can easily follow the ingoing portion of the vessel, that joins the outgoing portion in a common inter-

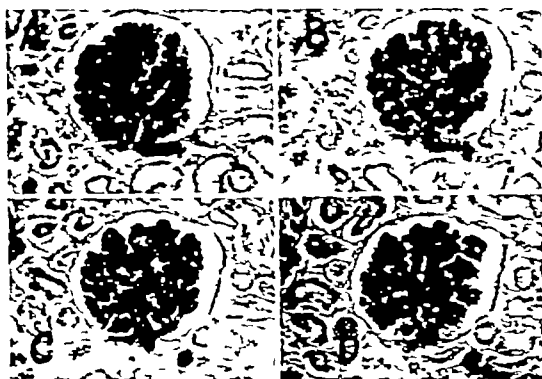


FIG 8 Sections in series of a glomerulus filled with India ink A shows habitual image of two vessels, but, if we thoroughly observe, we see that in B, C and D such vessels are no more than a single one from which endothelial arrangements shoot off

glomerular sinus, that is to say, the same vessel receives and allows the blood to flow from the way in to the way out of the glomerulus

Should a loop-like formation exist, between the afferent and the efferent vessels, the elaboration of a tunnel between one and the other, through hyaline tissue would be very difficult But if it is a single vessel instead, it is the glomerulus that has lost surface of sanguineous expansion, and that allows, so to speak, the blood to flow freely through all the vessels This blood flows freely in and out the glomerulus through a single vessel congenitally established and not worked out a posteriori

There would be another logical reason that might force us to think that the afferent and efferent vessels of the tuft are, instead of two different ones, only one vessel If we interposed a network between one vessel and the other, why should these two arterioles join like parallels? Bowman's capsule could surround the network with no need of the two vessels necessarily joining There is no anatomic or physiological reason for this to happen The only and logical reason is the following: it is one single vessel that folds upon itself as we have already said adopting the shape of a gun barrel

HISTOGENETIC PROOFS

Through Grünwald's and Popper's works (1940) we see in the renal blastema that a sanguineous lacuna develops out of a capillary lacuna that is surrounded

DIVERTICULUM OF THE URETER REPORT OF ANOTHER AUTHENTIC CASE

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True diverticula of the ureter are extremely rare. In 1947 one of us reviewed the literature, found 52 reported cases and discovered that 37 of them were not ureteral diverticula but represented 7 different types of unrelated anomalies (fig 1). Only 15 could be considered ureteral diverticula. Ten of these seemed to be of *congenital* origin, while 5 were associated with strictures, calculi or trauma and were thought to be *acquired* or false diverticula.

True and false types can be differentiated by their histologic structure. True diverticula are congenital and their walls contain all of the ureteral layers while the acquired forms consist of protrusions of the mucosa through the muscular coat and, therefore, lack any semblance of muscularis.

In 1947 one of us reported a case of true or congenital diverticulum of the ureter in which the sac contained 1600 cc (fig 2). In that same issue of the *Journal of Urology*, Piatt, Gahagan and Fischman reported 2 new cases. One of these followed ureterolithotomy and no doubt was an acquired or false diverticulum. An x-ray report was the only available evidence to support the diagnosis in their second case. Since there was no surgical or postmortem confirmation, that case must remain questionable.

In 1949, Mayers added the twelfth true ureteral diverticulum. Histologic description of the specimen was not given, but the author stated that "incision through the wall of the diverticulum revealed muscular hypertrophy." Most of the diverticulum was removed, the kidney was preserved and subsequent pyelograms were normal.

No other reports of ureteral diverticula were found in our review of publications during the past 3 years. We have another authentic personal case to add to this small group of congenital diverticula of the ureter.

CASE REPORT

(H. F. H. No. 570286) A white woman, aged 64, was admitted on the surgical service, April 3, 1949, complaining of a painless mass in the abdomen which had been discovered by her family physician whom she had consulted because of nervousness. The past history was noncontributory.

A large, firm, smooth, nonpulsating, freely movable mass occupied the right upper quadrant and right flank. The blood pressure was 175/80. Temperature and pulse were normal. No other gross pathological change was noted.

Laboratory studies revealed hemoglobin 12.5 gm, red blood cells 4.25 millions, white blood cells 7500, nonprotein nitrogen 32, negative Wassermann, normal liver function tests and normal urine. The electrocardiogram was normal.

Cystoscopy disclosed no vesical abnormalities. The left pyelogram was normal but a catheter could be inserted for only 14 cm. on the right (fig 3-1).

bends first in an obtuse angle and then in an acute angle, till both branches join simulating an afferent and efferent vessel within a zone, producing a multiproliferation of the irrigation and filtration surface, till it reaches the structure of the adult glomerulus

The embryologic metanephric demonstration is very important because it perfectly explains how a single capillary in formation, already become a sinus, will lead to the definite capillary glomerulus through the adaptation of the same vessel, through the bend in acute angle and through the surrounding of

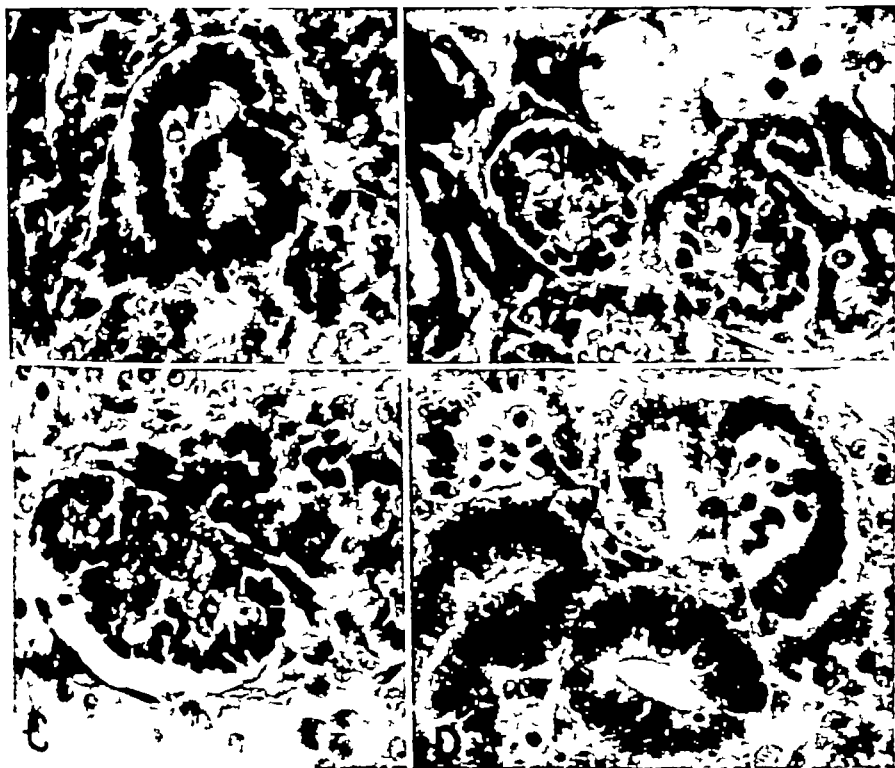


FIG. 9. A, metanephros of dog embryo. Sanguineous lacuna covered by mesenchyma, which already adopts shape of tubule with different walls to form Bowman's capsule. Central zone. B, another view of A. More central zone. C, same metanephros of A. More central zone than B. D, mesonephros of 17 days' old rabbit embryo.

this sort of cap of the acute angle of the vessel by all the other elements of the sanguineous lacuna, this lacuna has proliferated and has multiplied in its divisions and the whole has been surrounded by Bowman's capsule establishing the definite glomerulus. This fact observed in the metanephros can also be observed in the mesonephros.

In rabbit embryology we have been able to follow the evolution of the mesonephric zone and the mesonephric organ in all the different periods of the embryo. We also find facts that are categorical. The same thing occurs in the metanephros as in the mesonephros. Let us take this photomicrograph of a 17 days' old rabbit embryo. The mesonephric kidney is an organ that occupies most part of the embryo abdomen and whose evolution does not end but with

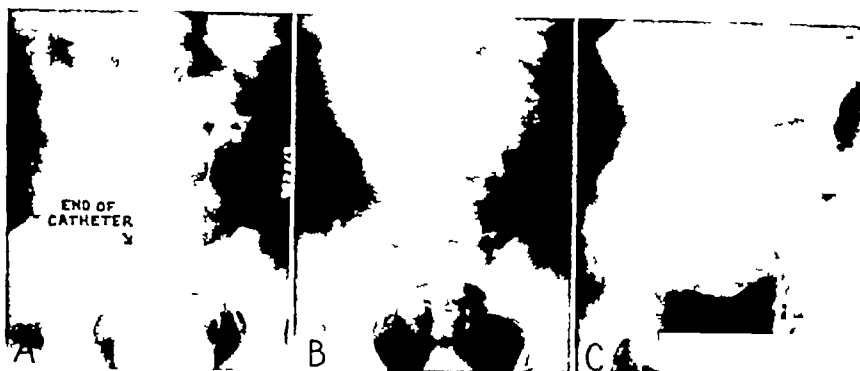


FIG 3 A, normal left retrograde pyelogram Catheter in right ureter passed only to lower edge of L5 Reflux of contrast medium from that point with nonfilling of right renal pelvis B, excretory urogram showing normal left kidney and no function on right C displacement of colon by mass in right side

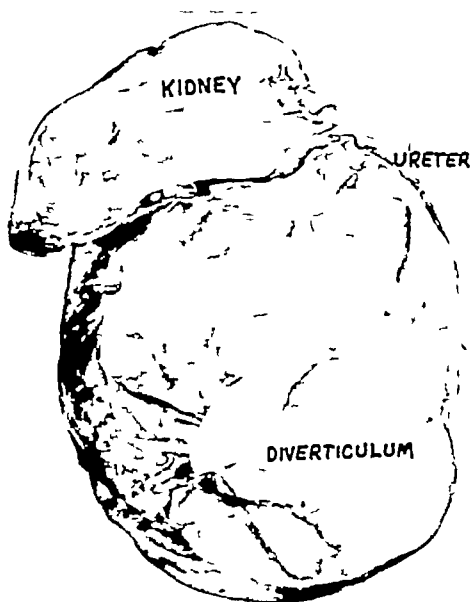


FIG 4 Photograph of surgical specimen Shell of kidney at top communicates with diverticulum through a short segment of ureter Note probe in ureteral opening Missing portion of diverticulum was left in situ and contained a second ureteral opening High lights on lining represent calcified plaques

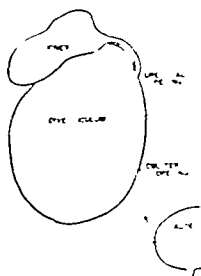


FIG 5 Diagrammatic reconstruction of ureteral diverticulum and its relationships

To begin with, we see that in all normal glomeruli, if we consider it according to the idea we have exposed, the afferent and efferent vessels place themselves like the barrel of a gun. That is to say that the stream that flows through the afferent vessel towards the glomerulus, by a simple hydraulic law, will tend to spread following the axis of such vessel and only when it will find the lacunar zone full, it will look for a way out through the other vessel placed parallel to the ingoing capillary. The same thing happens with the bend of a river, the stream tries to destroy the most convex coast, permitting currentless water to lie in inlets caused by the strength of the stream, that has always a tendency to follow the longitudinal axis of the river. The same interpretation is possible in the glomerulus. The sanguineous flood entering through the afferent portion has a tendency to follow forwards, flooding all the capillary lacunae of the glomerulus, once these are filled, it goes out through the efferent portion. On the other hand, if this conception of hydraulic force would not be enough, we must admit that there are some anatomical and physiological dispositions that will allow the blood to flow towards the glomerular capillary lacuna, in order to help in the filtration of all the elements that will form the urine and will also permit the continuity of the sanguineous stream towards the efferent vessel to return them to the general circulation.

We see that the afferent and efferent portions may have different caliber, especially under certain circumstances. We must think that the difference in diameter of both portions is due to a physiological adaptation in order to increase the glomerulus irrigation. If the afferent portion is the largest, undoubtedly a circulatory delay will be produced in the lacunar portion of the glomerulus. The delay will permit the repletion of the glomerulus with the blood provided by the afferent vessel and that will be, later on, carried off through the efferent vessel, producing a satisfactory glomerular filtration. This leads us to one of the most important conclusions of our findings, that is the harmony that exists between the relaxation and the contraction in the same vessel. This physiological harmony, dependent on the sympathetic system, has been observed in experiments performed with adrenalin chloride. Richards explains that small doses increase the volume of the kidney, and stronger doses produce the opposite effect: thus the diminution of its volume. Small doses increase renal filtration and strong doses abolish it. Here we might very well think, with the conception of a single vessel, that small doses help the contraction of the efferent portion of the vessel not only in the exit of the glomerulus, but also in the portion of the vessel that goes from the glomerulus to the renal tubule, that is to say: "the true portal arterial system of the kidney." When the vessel contracts it will undoubtedly produce the strongest sanguineous flood and an increase of the sanguineous ectasia within the glomerulus zone, thus helping the filtration. But if a stronger adrenalin discharge or other sympathetic stimulation phenomena occur, such as the phenomena described by Trueta or those produced with the staphylococic toxin, an absolutely different fact may happen: that is to say a lack of glomerular filtration. This lack of glomerular filtration may be determined by a total vessel contraction so much so that the caliber will

INTUSSUSCEPTION OF THE URETER ASSOCIATED WITH A BENIGN POLYP

HAROLD V. MORLEY, EDWARD J. SHUMAKER AND LAWRENCE W. GARDNER

This is a report of a record on a case of intussusception of a ureter due to a primary benign neoplasm. Previous cases of ureteral intussusception have been exceedingly rare, and very few references to this condition can be found in medical literature. Greater interest in recent years in primary tumors of the ureter has shown that they are perhaps less rare than was formerly considered, the benign type of ureteral new growth can still be considered uncommon enough to warrant addition case reports.

Hunner in 1938 reported a case of intussusception of the ureter due to a large papilloma-like polypus. A year later Bumpus reported an invagination of the ureter associated with what he believed to be a nonopaque calculus. Fagerstrom in 1947 included in a paper on proliferative tumors of the ureter a case report of ureteral intussusception associated with a benign papillary epithelioma. A few other writers, such as Edelstein and Marcus, have mentioned intussusception as a possible complication in ureteral neoplasms.

There have been several articles in the past few years which have adequately surveyed the literature in regard to the occurrence, classification, and treatment of primary ureteral tumors. Vest, Cooney, Edelstein, and Marcus have encouraged conservative surgery in selected cases of benign ureteral tumors. Theories as to the etiology have been adequately discussed by Fagerstrom, Ferris, Kaplan, and Thompson.

CASE REPORT

J. W. (No. 215722, Mount Carmel Mercy Hospital) aged 19, was first seen by us on December 29, 1949, because of the sudden onset of a sharp pain in the right costovertebral angle starting that morning. The pain radiated to the right upper abdominal quadrant and subsequently to the right lower abdomen without extension into the right testis. It was not associated with nausea, vomiting, or chills. The patient had no disturbance on urination. A similar episode had occurred in July 1949, six months previously, at which time pain in the right lower quadrant was followed by an appendectomy. Otherwise his past health had been excellent, and the patient gave no significant history except that in the past 6 months there might have been a little backache from time to time, but there were only the two incidents of any severe pain.

On physical examination the temperature was 99.8. The right kidney was not palpable although tenderness was noted in the right costovertebral angle and along the course of the ureter. The abdomen was soft and no masses were felt. The left kidney region was entirely negative. The external genitalia showed no abnormality and the rectal examination showed the prostate to be normal in

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through which the blood filters constantly to form the urine. It is easy to understand that the value of the sanguineous hygræmia, within the kidney would not suffer such considerable changes so as to deeply alter a vascular sector in this organ.

According to our proposed conception of the glomerulus, we can also explain, from the point of view of the normal physiology, the polyuria produced in some cases when the excitation or the sympathetic excitation phenomena cause a vaso-constriction of the efferent elements and a longer delay in the inter-glomerular circulation, therefore producing an increase of the sanguineous stagnation within Bowman's capsule, thus helping the filtration.

The pathological phenomena produced in the glomerulus can be also explained. In the first place it helps us to explain Trueta's "short-circuit" or "sanguineous diversion." It also helps us to interpret the presence of arterial blood color in the renal vein, observed by Claude Bernard and other later authors. We can also appreciate the anuria type produced after traumatism caused by Brwaters's and Bealle's phenomenon, in such cases the sanguineous flood will divert directly through the juxtamedullary glomeruli, even if Trueta interpretes it in another way in his works, owing to the traumatic damage and to noxious elements added to the sanguineous flood. Trueta and many former authors have established the following observations: the caliber of the afferent and efferent vessels is practically the same and, even in some occasions the caliber of the efferent vessel is greater than that of the afferent vessel thus determining the direct flow of sanguineous flood through the juxtamedullary zone and from there to the venules that the renal vein will form farther on. Under these circumstances the arterial type of blood appears through the renal vein. It is of course, blood that practically flows from the artery to the vein, that is to say blood that has not dropped its charge of oxihæmoglobin and whose oxygen has not been reduced. The only way of reasonably explaining this phenomenon is to think that there is a single vessel and a sanguineous glomerular lacuna adapted to it through evagination of this same vessel. It is impossible to think of an interposed network nor of a looping system interposed between one vessel and the other, the interposition of such a system would always give the idea of the flowing of the blood through these loops and this would produce urine constantly, even if the efferent vessel would be dilated. The increase of irrigation surface means increase in filtration surface and it would be practically impossible for it not to filter.

On the other side if there are tubular alterations such as the lower nephron syndrome that would produce occlusions in the renal tubules with glomerulus hypertrophy a deep alteration of the renal circulation would produce itself according to the former conception of the glomerulus so that we would have practically no blood left in the renal vein due to the glomerular compression. In our conception instead the renal circulation would be secured and we would see that in every acute state of kidney damage the blood would always flow from the renal artery and out through the renal vein passing through the capillaries. This would happen even if the compression due to the glomerulus hy-

tended portion of the ureter appeared to be filled with a large number of negative density shadows. Drainage films showed good emptying of the left kidney, but the megalo-ureter drained very poorly. The diagnoses entertained were either tumor, nonopaque stones, or blood clot filling the right ureter. An excretory urogram was done, and a normal left pyelogram obtained. No function was demonstrated on the right side until after 30 minutes when a nephrogram was obtained which showed no enlargement of the right kidney.

On January 3, 1950, a right lumbar incision was made and on exposing the kidney and upper ureter they appeared entirely normal. Seven centimeters distal to the ureteropelvic junction a large fusiform swelling with an intussusception of the upper portion of ureter was found. This fusiform swelling was approximately 2.5 cm. in diameter and extended beyond the reach of the original incision. On palpation the content of the swelling was thought to contain either a tumor or stone with more likelihood of a solid tumor mass. Since the length of the involved ureter, 11 cm., would not permit re-approximation of the two ends of a resected ureter a nephro-ureterectomy was decided on. The kidney was fixed and the pedicle clamped, cut, and tied. The ureter was cut and tied above the site of intussusception and swelling. The patient was taken from the position on his side and placed prone on the table, after which the skin of the abdomen was again prepared and patient draped, the incision was extended downward so that a complete nephro-ureterectomy could be performed.

The patient made an entirely uneventful recovery and has remained in excellent health since.

The specimen consisted of a kidney and a 24 cm. segment of the ureter.

The kidney weighed 140 gm. and measured 10.5 by 6 by 4 cm. The capsule was thin, translucent, and stripped with ease disclosing a greyish-brown, smooth external surface in which vague markings of previous fetal lobulations were identified. There was no evidence of pitting or other lesions. Bisection of the kidney disclosed a good cortical and medullary demarcation. The cortex varied from 4 to 6 mm. in thickness and the vertical striations were visualized. Medullary rays and the columns of Bertini were easily identified. The renal parenchyma presented no abnormality. The pelvis of the kidney was of normal size and there was no distortion of the major or minor calyces. These structures were lined by pinkish-grey, smooth mucosa in which no lesions were seen. There was no evidence of increased peripelvic fat.

The upper 7.0 cm. of the ureter presented a normal appearance. It averaged 3 to 4 mm. in diameter. Its wall averaged 1 mm. in thickness. The mucosa was pinkish-grey in color except for a few minute petechiae. Approximately 7 cm. from the ureteropelvic junction, there was a telescoping or intussusception of the upper portion of the ureter into the lower portion which was markedly dilated. The telescoped area measured approximately 1 cm. in length. The involved portion of ureter averaged 2.5 cm. in diameter and extended 11 cm. below the intussusception. Beneath that portion there was a 8.0 cm. segment of ureter averaging 5 mm. in diameter. The external surfaces of the dilated portion were pinkish-grey in color and contained numerous dilated blood vessels. Palpation

the glomerulus, establishes itself destroys the loops, the obliteration of the efferent vessel must be the rule, the hyalinization must be the corollary. The afferent vessel will only go on functioning if it is a single vessel with the efferent, so that, even if the glomerulus hyalinizes itself and the sanguineous lacuna disappears, the circulation will be secured by the same glomerular vessel, because it is a single one.

If the glomerulus were destroyed through inflammation and sclerosis there was such an urgent need, in pathology, for an explanation of a blood diverting system explaining why the sanguineous circulation was not altered, that Goormaghtigh has described, perhaps a little capriciously, a diverting system a shunt as Bieder calls it, that diverts the blood from an afferent vessel to an efferent vessel. No "shunt" is established, it is the circulation that evidently establishes itself since the filtering portion atrophies and only the circulating portion is left between one end and the other of the vessel. The existence of Bieder's and Goormaghtigh's system is not absolutely necessary. It is simply the same vessel that transforms itself, due to the pathological circumstances of the glomerulus.

SUMMARY

In opposition to the actual anatomical conception of the structure of the glomerular tuft, the authors demonstrate that this glomerular tuft is formed by a single vessel, bent in an acute angle, and that the tuft is the same wall of the vessel that through evagination, has subdivided itself in multiple blind ending acicular tubule arrangements, all of them joining in a common sinus.

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hydropic degeneration, resulting in multiple cyst formation, no evidence of malignancy, intussusception of ureter above tumor, dilatation of ureter by polyp, hypertrophy of ureteral wall, moderate cloudy swelling of ureteral parenchyma, few submucosal petechiae in pelvis

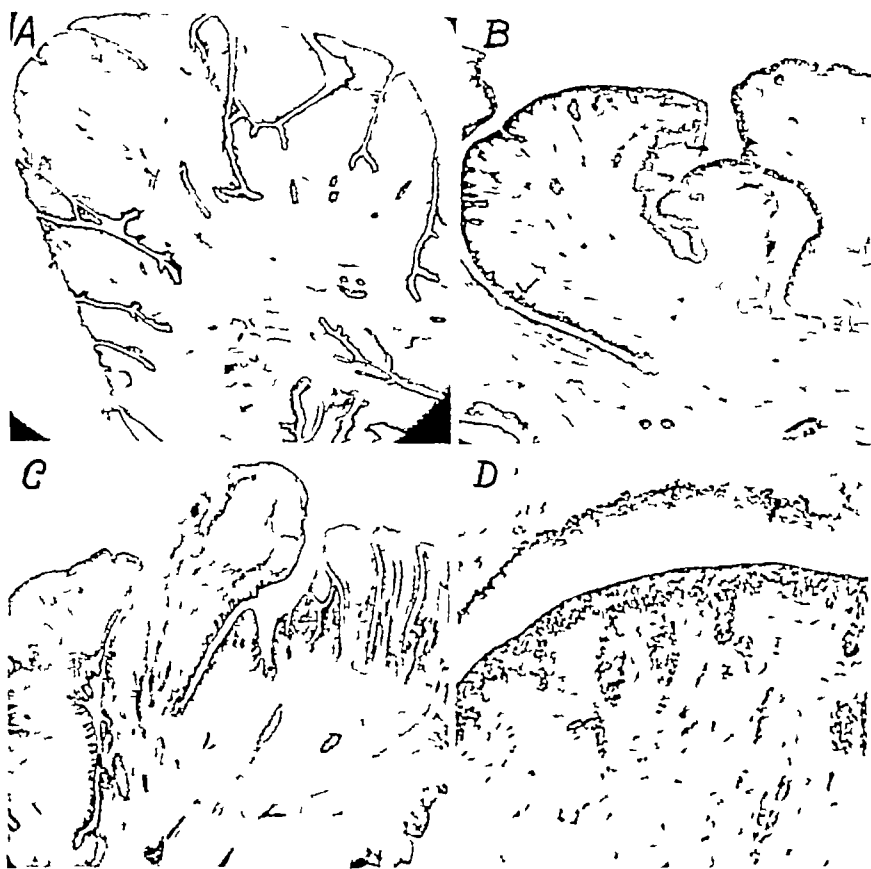


FIG. 3—A, cross section of polyp illustrating papilliferous form. B, segment of polyp. C, segment of polyp illustrating cyst like spaces. D, segment of polyp illustrating transitional epithelial covering and fibroblastic matrix.

COMMENT

The preoperative diagnosis of this benign polyp was not made though the diagnosis of tumor was one of the first to be considered. There was no palpable tumor mass nor had the patient seen any blood in the urine. Pain was the prime complaint and had occurred on two occasions. The first episode of pain ended in an appendectomy. The second attack of pain, 6 months later, resulted in a urological investigation. The pain was quite characteristic of ureteral colic, but there were no findings that were pathognomonic of tumor alone. The cystoscopic examination revealed a normal bladder. The tumor was attached too high and did not extend down far enough to present any findings at the ureteral orifice. An obstruction was met and could not be overcome on catheterization of the

all of the minor calyces with ease. Calculi or their fragments are dislodged by the fluid jet and/or the movements of the cannula tip, and are then washed forcibly out of the pyelotomy incision. Fragments and calculi are recovered on gauze held around the pyelotomy wound and the fluid is removed by continuous suction.

CONCLUSIONS

The assembly of these previously unrelated irrigating devices has provided a most efficient instrument for lavage of the renal pelvis. The component parts are readily available at low cost from any surgical equipment house. The resulting instrument is easily sterilized and can be kept permanently available, eliminating the confusion and consternation which so frequently accompany efforts to irrigate the opened kidney pelvis.

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SPONTANEOUS OR NONTRAUMATIC EXTRAVASATION FROM THE URETER

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A surgical problem of immediate and grave significance is always precipitated by extravasation of urine. Although it may occur at any level of the urinary channel, in no part of the whole tract is it so uncommon as from the ureter. The latter would seem to be immune to injury because of its size and location. Rupture of the ureter may result, however, from external trauma, from surgical injury in the course of operations on adjacent structures and from cystoscopic ureteral manipulation. Although these accidents may occur, they have been infrequently reported. Extravasation of urine due to injury of the ureter which occurs in the absence of any of the above forces is even more unusual and has been referred to as nontraumatic or spontaneous extravasation of the ureter. An outline of 27 such cases is presented in table 1 which includes 26 previously reported in the world literature, and one of mine whose case report follows.

Beekman-Downtown Hospital No. 51389, W.B., a 42 year old white man, was admitted to the hospital 1 hour after the sudden onset of right loin pain. The latter was deep seated, persistent, knifelike and occasionally radiated to the right testicle. There were no accompanying urinary symptoms. The past history was negative and there was no prior trauma to the abdomen or loin. Examination revealed him to be acutely ill, the temperature was 103°F and the pulse rate 122. There was some degree of circumoral pallor. Palpation of the left loin was negative. There was exquisite tenderness to percussion in the right loin. This area was too spastic to permit of satisfactory palpation. The abdomen was moderately distended. Diffuse tenderness and voluntary rigidity in the right half were present with rebound tenderness in the lower quadrant. Rectal examination revealed indefinite tenderness and fullness above the prostate on the right side. The voided urine disclosed 75-100 red blood cells per high power field, a trace of albumin and numerous uric acid crystals. The white blood count was 26,500 with a marked shift to the left. The blood nonprotein nitrogen was 26 mg. per cent, the blood uric acid 7.2 mg. per cent. The history and physical findings suggested a differential between a right ureteral calculus with an obstructed infected hydronephrosis, and a perforated retrocecal appendix.

A simple abdominal film obtained soon after admission revealed both renal shadows to be of normal size and in good position. A small calcareous shadow 2 by 3 mm. was visualized just above the right ischial spine which conceivably could be in the course of the right ureter. Emergency excretory urography was then performed. Following the intravenous injection of diodrast there was prompt excretion and visualization of a normal left pelvis and ureter. Excretion of the contrast substance was delayed on the right side. On the late film (fig. 1, 1) the pelvis appeared to be slightly dilated, and just below the ureteropelvic junction there was seen a collection of extravasated contrast material. The bladder at-

The right kidney appeared to be greatly enlarged, occupying almost the entire right side of the abdomen. A chest radiograph showed only some elevation of the right side of the diaphragm.

On July 14, under local anesthesia, cystoscopy was performed. An 21F cystoscope passed easily. The bladder was normal. Ureteral catheters were passed, the right one going up only part way. There was good flow of urine from the left side, but none from the right. A retrograde pyelo-ureterogram showed the right ureteral catheter lying in a tortuous ureter and obstructed at L4 (fig 1). No dye entered the right renal mass. Culture of bladder urine showed *B. coli*.

Examination on July 18 showed essentially the same findings. The mass appeared fluctuant and needle puncture obtained 100 cc of creamy pus, which on culture showed a heavy growth of coliform bacilli only. Repeated examina-

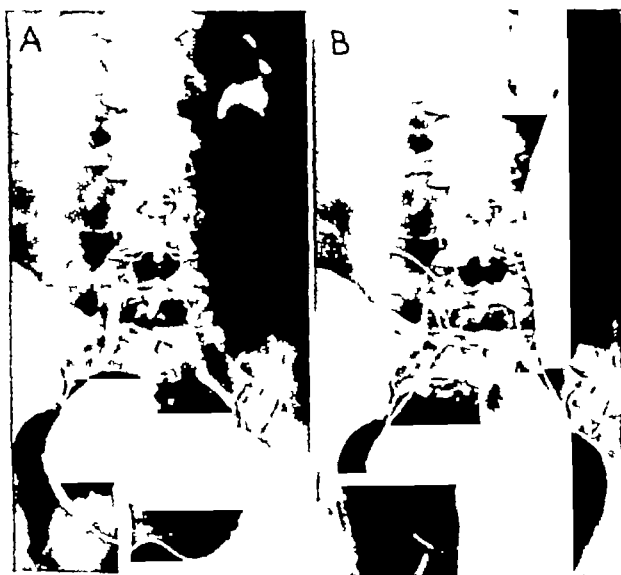


FIG 1. Retrograde pyelo ureterograms show tortuosity of right ureter and obstruction at L4. Large mass occupies right side of abdomen.

tion of 24 hour urine specimens did not reveal any tubercle bacilli. On July 20, the right kidney was explored through a lumbar incision. The muscle layers were compressed into one thin, tense layer by a large tumor mass. Aspiration of the tumor again revealed thick pus, and as much of this as possible was removed. No definite kidney structure was seen. Great difficulty was encountered in trying to free this renal mass from surrounding structures, including the peritoneum. On opening further into the tumor, a large quantity of papillary, reddish-yellow, soft material was encountered. This was believed to be extensive papillary carcinoma invading the perirenal space. This material could be traced down the lateral and posterior walls to the pelvis and was adherent to the peritoneum. The entire mass of tissue was removed with as much of the infiltrating tissue as possible. A gauze packing was inserted to control the oozing and the incision was closed.

TABLE 1—Continued

AUTHOR	SEX AGE	PREVIOUS HISTORY	IMMEDIATE HISTORY	URINARY SYMPTOMS	DURA- TION	PHYSICAL FINDINGS	URINARY REPORTS	CYSTOSCOPY RETROGRADE	SITE OF CALCULUS	FINDINGS AT OPERATION	SITE OF RUPTURE	OPERATIVE TREATMENT	END RESULTS
9 Foulds Varey —1934	M 29	Negative	It lt loam pain	Negative	7 Dys	Mass tender mass lt loam	Negative	Indwelling ureteral cath No retrograde	Lower Ureter	Large retro peritoneal abscess	It Lower Ureter	I & D	Good
10 Foulds Varey —1934	M 53	Negative	Lt loam pain	Negative	9 Hrs	Rigidity ten- derness lt lower quad- rant	Pyuria	Not done	Lower Ureter	Perinephric abscess	It Upper Ureter	I & D	Good
11 Foulds Varey —1934	M 30	Transplanta- tion ureter to sigmoid	Chills lower Passed Calculus	Frequency Passed Calculus	4 Hrs	Rigidity lt lower quad- rant Disten- tion	Pyuria	Not done	Lower Ureter	Extravasation	It Lower Ureter	I & D	Died An- topsy— Retropri- etoneal Phlegmon Good
12 Friedman —1935	M 62	Prostatec- tomy 6 mos	Rt loam pain	Negative	6 Dys	Mass tender mass rt loam	Negative	Not done	Outside Upper Ureter	Extravasation	Rt Upper Ureter	I & D	Good
13 Conlin —1936	F 31	Rt renal calic 3 yrs	Rt Renal Calic	Negative	2 Dys	Tenderness Mass rt loam	Pyuria	Not done	Outside Upper Ureter	Malary ab- scesses of kidney Ure- ter avulsed	Rt Upper Ureter	Nephrectomy	Good
14 Surmeo —1937	—	Negative	Abdominal pain	Negative	4 Ds	Tenderness Mass rt loam	Pyuria	Extrava- sation	Upper ureter	Not done	Rt upper ureter	None	Good
15 Surmeo —1937	—	It renal calic	Abdominal pain	Not Re- ported	—	Not stated	Pyuria	Extrava- sation	Upper ureter	Extravasation non fune- kidney	Rt upper ureter	Nephrectomy	Good
16 Surmeo 1937	—	It renal calic	It renal calic	Not Re- ported	6 Dys	Mass lt loam	RBC's	Extrava- sation	Upper ureter	Not stated	It upper ureter	Not Stated	Not Re- ported Good
17 Surmeo 1937	—	Rt renal calic	Abdominal pain Colic	Not Re- ported	—	Not stated	Not stated	Extrava- sation	Upper ureter	Not done	Rt upper ureter	None	Good
18 Surmeo 1937	—	Rt renal calic	Abdominal pain Colic	Not Re- ported	—	Not stated	Not stated	Extrava- sation	Lower ureter	Not stated	Rt lower ureter	Not Stated	Not Re- ported
19 Surmeo —1937	—	Negative	Rt renal calic	Not Re- ported	2 Wks	Mass lt loam	Pyuria	Extrava- sation	Upper ureter	Not stated	It upper ureter	Not Stated	Not Re- ported
20 Curtis —1938	M 17	It renal calic	It lt loam pain	Not Re- ported	4 Hrs	Tenderness Mass lt loam	Negative	Extrava- sation	Upper ureter	Extravasation of scar Ab- scess	It upper ureter	I & D	Good

DISCUSSION

The course of events in this unusual case can be fairly accurately conjectured. A hydronephrotic, nonfunctioning kidney became infected, probably by an ascending infection from the bladder, although a metastatic route must be considered. Pyonephrosis resulted, with the formation of foam cell granulomatous tissue. This tissue infiltrated the perirenal space, extending from the diaphragm to the pelvis and adhering to the peritoneum and adjacent tissues. The onset of the present illness was heralded by urinary burning and hematuria. Normal temperature and white blood cell count were noted.

The question of a possible tuberculous etiology arises in view of the history supplied by her own physician. Acid-fast bacilli were only reportedly found on one occasion and further studies did not substantiate this. Thorough search in this hospital did not reveal any tuberculous infection. Histological examination of many sections of the tissue removed at operation showed no evidence of tuberculosis, and indeed, the dense, regular reticulin formation (fig. 2, *B*) supports this.

SUMMARY

A general review of "foam cell" reaction to suppuration in the kidney is given.

The case report of an unusual granuloma of the kidney is given in detail. Being mistaken for infiltrating tumor in this case and for tuberculosis in several other reported cases are noteworthy points.

Reported cases of this condition are rare, and none so extensive could be found.

We wish to thank Dr. Todden, of the Department of Pathology, Dalhousie University Medical School, for his invaluable and patient instruction in elucidating the underlying pathology. The photographs were taken by Mr. Merrimen, of the department of medical photography of Camp Hill Hospital.

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self was of normal configuration but the right lower ureter was never visualized. Cystoscopy was done immediately. The bladder was negative. The right ureteral orifice which had a normal appearance was catheterized without obstruction for a distance of 10 cm using an 6F ureteral catheter. No urine drained from this side. X-rays were then taken with the patient in Trendelenburg position. A simple film with the catheter in position revealed that the previously described calcareous shadow was outside the course of the ureter. Retrograde pyelogram obtained by the instillation of 20 cc of 17 per cent skiodan by the gravity method disclosed a large area of extravasated contrast material extending under the



FIG. 1. *A*, 60 minute film of excretory urogram series. Demonstrates dilated right renal pelvis, loss of continuity at ureteropelvic junction and collection of extravasated contrast material below and to right of ureteropelvic region. *B*, retrograde pyelogram performed using gravity method with patient in Trendelenburg position and catheter in lower portion of ureter. Demonstrates large area of extravasated contrast material extending from ureteropelvic junction to lower pole of kidney. Remainder of ureter appears normal. *C*, trapping film taken 10 minutes after *B*. Demonstrates that area of extravasation appears to be greater in extent, and although ureter appears normal, none of retrograde material has entered bladder.

lower pole of the kidney from the ureteropelvic junction (fig. 1, *B* and *C*). The configuration of the pelvis, calyces and the lower ureter appeared to be normal. A diagnosis of rupture of the right upper ureter or ureteropelvic junction was made and immediate exploration of the loin advised.

At operation, the muscles and fascia were found to be edematous. Two quarts of clear urine were aspirated from the right loin area. Careful exploration revealed that the kidney and its pelvis were normal. A ragged rent measuring 7.5 cm through which urine exuded was found 1.5 cm below the ureteropelvic junction. No calculus or induration could be palpated in the pelvis or the upper ureter. The perforation was not sutured. The retroperitoneal area was drained by means of several Penrose drains. The anterior half of the wound was closed in layers. The posterior portion was left open.

When the right side was injected, the renal pelvis could not be visualized and only the lower ureter filled. When a bulb pyelogram was attempted, only the lower half of the right ureter was demonstrated. With excretory urography

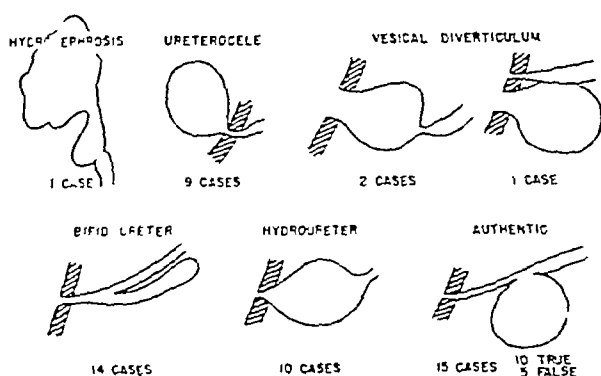


FIGURE 1

FIG. 1. Types of anomalies that have been reported in early literature as diverticula of ureter.

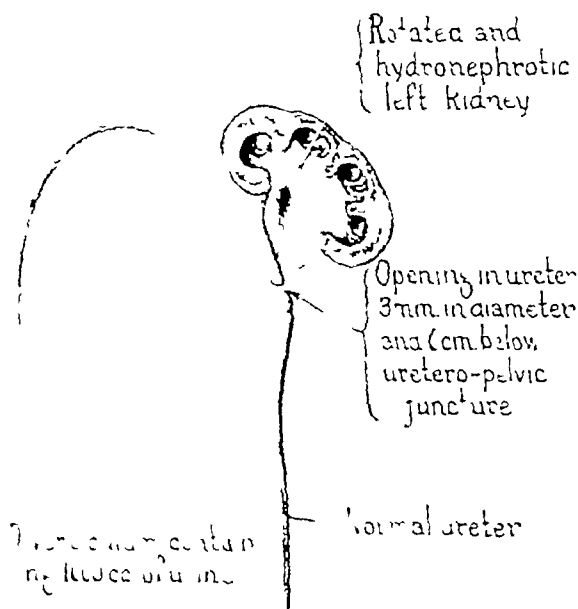


FIG. 2. Our first case of ureteral diverticulum reported in 1947.

there was prompt appearance of the dye on the left and no evidence of function on the right (fig. 3 B).

Barium enema showed displacement of the colon (fig. 3 C). The mass was thought to be of renal origin but the type of lesion was most uncertain. The tentative diagnosis was tumor of the right kidney.

On April 9 the patient was explored through a subcostal incision. The contents of the peritoneal cavity proved to be normal. The hepatic flexure of the

paroxysmic pain which was noted in 23, in the remaining four, a constant dull ache was experienced, 3) intense, prolonged contraction of the corresponding hemi abdomen. This was found in 15 cases and suggested the possibility of an intra peritoneal lesion. A toxic or hemorrhagic picture is soon added to the foregoing. These cases have a final common anatomic picture, the perinephric phlegmon, the basis of which is the serohematic or urinary extravasation. These patients appeared to be more acutely ill and their temperature and white blood counts were elevated to a greater degree than one would expect with an uncomplicated ureteral calculus. The striking fact was the paucity of urinary symptoms and urinary findings at the time that the patient came under observation. Frequency and urgency of urination were noted 3 times, dysuria and gross hematuria once. One patient had passed a ureteral calculus while another had not voided for several days before admission to the hospital.

Physical examination revealed that all but one of the patients appeared to be acutely ill. Percussion tenderness over the affected loin was positive in 23. Although extravasation of urine was present in all, a localized palpable mass was found in 15. In 10, the mass was felt in the corresponding loin and led to a preliminary diagnosis of a perinephric abscess. In the remaining 5 patients, it was found in the lower quadrant of the abdomen. Rigidity with rebound tenderness of the corresponding half of the abdomen was noted in twelve. Although the latter was suggestive of extravasation of urine before a definite diagnosis was established, a differentiation from an intraperitoneal lesion was difficult in the absence of further urological investigation. A preliminary diagnosis of appendicitis was entertained in 6, intestinal obstruction in 3 and a ruptured ectopic in 1.

A report of the urine analysis is available in 24 cases. It was completely negative in 7 patients. Gross hematuria was found in 1 while albumin and microscopic hematuria was seen in 6. Varying degrees of pyuria were noted in 10, uric acid crystals in 1.

The diagnosis of spontaneous perforation of the ureter should always be considered if the symptoms and physical findings of ureteral calculus are encountered in a patient who appears to be more seriously ill than is usual. Similar suspicion should be directed to those conditions in which the abdominal signs point toward an intraperitoneal lesion but in which the history and physical findings suggest a renal involvement. A simple abdominal film may give valuable information. This includes localization of the calculus, if present, blurring of the psoas shadow on the affected side and identification of a mass at the lower pole of the kidney. Excretory urography is disappointing in the majority of the cases since there is failure of the affected kidney to excrete the contrast substance. It should be done, however, as valuable information is usually obtained concerning the contralateral kidney since excretion is usually normal on this side. Occasionally, one may be fortunate in demonstrating extravasation from the ruptured ureter. Excretory urography was performed on 6 patients in this series. In one no excretion of the contrast substance appeared on either side. In three, excretion was excellent in the contralateral kidney, while visualization was not obtained on the involved side. Extravasation of the contrast material was demonstrated on the affected

colon was freed and retracted medially after which the mass was discovered retroperitoneally. It extended from under the costal margin to the pelvic brim, was irregular, tense, hard in some areas and very adherent. On the antero-medial surface was the thin-walled kidney.

The mass was opened accidentally and a large amount of dark brown fluid escaped. With suction, 950 cc of additional fluid were evacuated from the huge cavity. The total capacity remains obscure but it far exceeded that of our previous case (1600 cc).

The lining of the single large cavity was studded with calcified plaques. On the medial aspect there was a small opening which proved to be the opening of the ureter (fig. 4). Lower in the sac was an indentation which coincided with the upper end of the catheterized portion of the ureter. In this area the wall was densely adherent to the vena cava and adjacent structures. This part of the diverticulum and the lower ureter were left in situ, but the remainder was excised, along with the attached right kidney.

The retroperitoneal space was drained through a stab wound and the incision was closed with catgut in the peritoneum and silk in the muscles, fascia and skin.

The gross appearance of the specimen is shown in figure 4. A thin layer of renal parenchyma forming part of the wall of a dilated cavity was the only remnant of kidney. The upper segment of ureter was dilated and opened into the diverticulum 9 cm below the ureteropelvic junction. The wall of the diverticulum was 1 to 2 mm thick and the lining was covered with small calcium deposits. The missing portion of the sac wall contained the other communication with the ureter. As the diverticulum enlarged, pressure and calcification apparently obliterated the opening.

Sections of the wall of the diverticulum showed striated muscle and dense collagen bundles. The calcification penetrated to varying depths. Sections of the kidney showed only a few isolated and sclerosed glomeruli.

Figure 5 is a diagrammatic reconstruction of the anatomic relationships. The final diagnosis was congenital diverticulum of the right ureter and secondary hydronephrotic atrophy of the kidney.

The patient's postoperative course was entirely uneventful. She left the hospital 13 days later and has had no further abdominal complaints.

SUMMARY

Another case of true congenital diverticulum of the ureter has been added to the 12 in the literature.

This diverticulum was one of the largest on record, had completely destroyed the kidney, and was unique because it contained numerous calcified plaques.

The patient recovered after diverticulectomy and nephrectomy.

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ods. In the majority of the cases the calculus becomes impacted in the region of the ureteropelvic junction or in the lower ureter. Subsequent peri-ureteritis, spasm and localized necrosis in the occluded segment may then lead to actual perforation. In a small number, the calculus causes injury to the upper part of the ureter, commonly at the ureteropelvic junction and then passes down the ureter, only to produce obstruction low down with increased pressure above and consequent rupture at the injured area.

The place of the rupture in the spontaneous case differs from the direction of the line in the traumatic ruptures. In the spontaneous cases, the rupture occurs in the pyelo-ureteral course and in the segments corresponding to the anatomic narrows. In the traumatic cases, the rupture takes place at the insertion of the calyx or the parenchyma and the line includes at the same time the calyx and the posterior renal surface. This explains why in spontaneous perforation of the ureter, the extravasation from the first moment is intimately related to the peritoneum and produces the gross abdominal symptomatology so characteristic of peritoneal irritation.

In this series of 27 cases, operative intervention was undertaken in nineteen. Five patients were either not operated upon or refused surgery. The type of treatment instituted in three cases is not stated. The operative findings are known in 19 cases. Extravasation of urine was found in all. Localization to form an abscess was seen in thirteen, it was high in seven, low in four and extensive in two, extending from the lower pole of the kidney to the iliac crest. Extravasation of urine without definite abscess formation was noted in six. Two of these were associated with markedly infected kidneys.

Incision and drainage of the loin and/or the lower retroperitoneal area was performed as a primary procedure at the time of exploration in 16 patients. In addition, at this time, the calculus was removed in two instances. In the first, the calculus could easily be palpated at the site of ureteral perforation and was removed by ureterolithotomy. The second patient was cystoscoped preoperatively and the calculus pushed up into the kidney. It was then removed through a nephrotomy opening at the time of incision and drainage. Two patients were acutely ill on admission. They were treated with indwelling ureteral catheter preoperatively in order to improve the renal function of the affected kidney. This expedient was unsuccessful as in both instances the operator felt compelled to do a nephrostomy because of failure of the kidney to regain its function at the time of incision and drainage. In none of the cases in this series was either the perforation sutured or a splinting catheter used. One patient had a persistent urinary fistula weeks after the original incision and drainage. The fistula was excised at a later date with a good result. A primary nephrectomy was done 3 times, in two, because of marked suppuration of the kidney and in the third because of avulsion of the ureter from the pelvis. A secondary nephrectomy had to be done in 3 patients. In one at the time of incision and drainage the ureter was found traversing a large abscess. Despite postoperative dilatation and ureteral catheter drainage the affected kidney never regained its function and was subsequently extirpated. In the second, a rupture at the ureteropelvic junction was treated by

impacted ureteral calculus. The second died with extensive gangrene of the retroperitoneal area despite incision and drainage.

The remaining 21 patients in this series recovered. Four individuals were treated conservatively and had a good end result. The remaining seventeen were subjected to operative intervention. Three had a primary nephrectomy as previously stated. Incision and drainage of the loin or the lower retroperitoneal area was carried out in the other fourteen. Persistent suppuration and failure of kidney function to return in the affected kidney in two, and re-rupture of the ureter in one, necessitated a secondary nephrectomy in three of these cases. The postoperative course in the remaining eleven was uneventful except that one required a secondary excision of a persistent ureteral fistula. The operative wounds healed well and the kidneys demonstrated a normal radiological and functional appearance in the follow-up period. The ureter was also normal and there was no evidence of stricture at the site of original rupture.

Although the end results are good in four of the 5 patients who had no operative intervention, the latter is not advised as the cases usually have a protracted morbid course. In addition, one is faced with the constant threat of death from retroperitoneal phlegmon and sepsis. Once a diagnosis of extravasation from the ureter is established, immediate exploration is indicated. The simplest procedure yielding the best results in the majority of the cases is incision and drainage of the loin and/or the lower retroperitoneal area. If the offending calculus is readily palpable, it may be removed, but any deep exploration would seem to be both unnecessary and hazardous. A primary nephrectomy would also appear to be infrequently indicated in the light of our experiences with the newer antibiotics and should be reserved for those instances in which there is marked destruction of the kidney and/or the ureter. Preoperative ureteral catheter drainage in order to improve the function of the affected kidney would seem to be unwise. Much valuable time is lost and much better results can be expected by immediate and adequate drainage, decapsulation and pyelostomy in these instances. Repair of the perforation is unnecessary as it healed in every instance in this series without this procedure. Although no author in this series used a T tube or splinting catheter, these aids might be utilized to good advantage in those cases with a wide loss of ureteral substance. Postoperative cystoscopic dilatation of the ureter in an attempt to facilitate passage of the calculus is an unnecessary procedure in these cases. No problem relating to the calculus was noted in any of these patients in the postoperative period.

SUMMARY

A case of spontaneous or nontraumatic extravasation from the ureter has been reviewed and added to the 26 previously reported in the world literature.

A study of these cases reveals the absence of any trauma or pre-existing disease in the urinary tract. Spontaneous rupture of the ureter is invariably secondary to pyelo- or ureterolithiasis since a calculus could either be demonstrated or recovered in 23 of these cases.

Clinically these patients are more acutely ill than one would expect with an

of the specimen disclosed a cystic sensation. The specimen was opened longitudinally and in the area of dilatation, there was a 10 by 2 cm pedunculated tumor (fig. 2). The pedicle was found in the area of intussusception and measured 4 mm in diameter. Externally the tumor presented a somewhat papilliferous pattern with a somewhat mosaic-like pattern in certain areas. The tumor was grey in color and further characterized by the presence of numerous translucent cystic areas varying from 2 to 8 mm in diameter, which were most numerous in the inferior third. These structures were filled with a clear watery fluid. Serial cross section of the tumor disclosed a centrally placed grey core, varying from 2 to 4 mm in diameter containing dilated blood vessels. From this core there were radiating processes of somewhat smooth external outline. These processes varied from 5 to 10 mm in height and 2 to 4 mm in thickness. Apparently areas of cystic degeneration were present giving rise to the previously noted translucent cyst.



Fig. 2. A: ureter opened longitudinally with pedunculated polyp. Intussusception of ureter above tumor. B: schematic drawing, showing intussusception of ureter associated with benign polyp.

The microscopic sections (fig. 3) consisted of an unusual ureteral tumor in which the cross-sectional architecture under low power magnification, disclosed various shaped processes radiating from a central core. The structures were knob-like, sharp or rounded, and were covered by transitional epithelium which in some areas was thinned or atrophic. No evidence of hyperchromatism was noted. The epithelial elements were of quiescent type. The remaining portion of the polyp was composed of a pink staining collagenous-like substance which in the peripheral portion possessed a loose texture. The latter suggested hydropic degeneration. Only a few cellular elements were identified. Some were spindle in form while others were stellate. In some areas immediately beneath the epithelium there were large zones of hydropic degeneration resulting in the production of cyst-like spaces. No evidence of a distinct lining was seen in the structure. A few lymphocytes and histiocytes were noted beneath the epithelium in some areas. The central portion of the tumor was composed of a more compact, relatively cellular tissue of collagenous type.

Section through the narrow pedicle revealed only a collagenous stalk which ultimately blended with the normal ureteral wall.

No significant histopathological changes were observed in the kidney proper (findings). An unusual fibrous polyp of the ureter undergoing extensive

URETERO-INTESTINAL ANASTOMOSIS

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A résumé of our studies on uretero-intestinal anastomosis 11 years ago revealed that "the use of the intact ureter during the first stage of the operation has simplified the ureteral submucosal attachment to the bowel." The best method of producing a permanent uretero-intestinal orifice during the second stage needed further investigation. In a later publication (1942), we discussed late uretero-intestinal stenosis of the new ostium. It was stated that if the ureteral and bowel mucosa remained opposed without intervening scar tissue, the new mucosal orifice would not contract and remain permanently patent. Our studies also revealed that "an excessive amount of free ureter projecting into the bowel lumen could predispose to infection and constriction of the new ureteral orifice, resulting in hydronephrosis and renal insufficiency."

Since that time a great deal more has been written on the subject and many new techniques have been presented. The most revolutionary concepts have been presented by Nesbit and by Cordonnier. These authors believe that the establishment of a preliminary bowel sphincter or the use of a tunnel is no longer necessary. The object of this paper is to present additional laboratory and clinical experiences in ureterocolic operations. We have found the Nesbit spatula type of oblique attachment very simple and practical. We, however, have also noted that after the Nesbit operations there is no renal protection and severe infections and ureteral reflux may be observed. Our studies further indicate that, even in presence of good urinary drainage, varying degrees of chronic renal infections following uretero-colic operations are exceedingly common. These infections may result in azotemia, renal insufficiency and death.

MUCOSA-TO-MUCOSA

The first direct mucosa-to-mucosa attachment of the ureter to the bowel was carried out by Smith in 1878 and Chaput in 1892. The mucosa of the ureter was first sutured to the mucosa of the bowel and a second line of sutures closed the muscular and serous layers of the bowel around the ureter. The anastomosis was completed by closing the bowel wall over the distal transplanted ureter. A lateral mucosa-to-mucosa anastomosis, without a tunnel, was described by Peterson in 1900. He united a slit in the side of the ureter with an adjacent slit in the bowel of a dog. He was not successful in preventing infection or ureteral dilation. In 1909, Mirovotseff modified Tischoff's technique of overlapping muscle and sutured the end of the ureter directly into the window of the bowel. Following the attachment the ureter was enclosed by overlapping rectal wall.

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Appreciation is extended to Drs Cyril H. Hauser, John L. Bell and Harold L. Method for their valuable assistance in the consummation of this experimental study.

Abbott Laboratories furnished the sulfonamides and antibiotics which were used in these experimental studies.

ureter. The x-ray findings as described demonstrated a nonopaque filling of the dilated ureter but were not diagnostic of tumor. No tumor cells were demonstrated in the urine. The findings were sufficient to warrant operative intervention. Hamm and LaValle, in their recent report of tumors of the ureter, found no recognized signs and symptoms characteristic of ureteral tumor.

At the time of operation consideration was given to attempting a conservative procedure in order to save the kidney, but the amount of ureter which appeared to be involved and the possibility that this was not entirely benign led to the nephro-ureterectomy. No frozen section was taken. The age of this patient, nineteen years of age, was much younger than the majority of the cases reported which are most commonly found in the fourth, fifth, sixth and seventh decades; this also was a factor in one's desire to conserve the kidney. However, on the other hand should it have proven a malignant tumor, its rate of spread would in all probability have been extremely rapid. O'Connor in 1949 pointed out the difficulty of making a diagnosis of benign tumor of the ureter and recommended radical excision as early as possible as the treatment of choice.

The narrow pedicle by which this relatively large, benign new growth was attached undoubtedly was the big factor in causing the intussusception of the ureter. By the same token the intussuscepted ureter made more complete the obstruction and perhaps made a preoperative diagnosis more difficult.

CONCLUSIONS

A report of an intussusception of a ureter associated with an unusual fibrous polyp is added to the literature.

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closed in layers. The skin was carefully approximated with a subcuticular closure. Postoperative dressings were not used. There were no serious wound infections. Postoperatively 150,000 units of intramuscular penicillin and 0.25 gm oral streptomycin were given daily for 7 days. In addition, oral sulfadiazine and sulfathiazole tablets, 0.15 gm each, 3 tablets daily, 3 days a week were



FIG 1. Two stage ureterosigmoidostomy, intact ureter first stage, and open bowel anastomosis during second stage. *a*, Intact ureter divided 2 cm below point where it egressed from bowel attachment. *b*, Small bowel fistula made just below distal ureteral attachment. *c*, Excess ureter projected into bowel lumen. *d*, Fistula closed with interrupted silk sutures. *e*, Excess ureter resected and ureteral mucosa accurately sutured to bowel mucosa with 00000 chromic sutures. *f*, Bowel incision closed. Mucosa closed with continuous 00000 chromic and muscularis and serosa with interrupted silk. The foregoing technique gave best results in dogs.

administered indefinitely. Follow-up pyelograms were made with 20 to 25 cc intravenous diodrast solution. The pyelograms were traced from the films and reproduced by the artist for better presentation and printing. Blood chemistry studies were made at irregular intervals.

GROUP 1. TWO STAGE OPERATION, EXCESS URETER TURNED INTO BOWEL, 3 DOGS

It has previously been noted by us that if an excessive amount of ureter is turned into the bowel lumen, stenosis of the ostium may ensue. The large amount of ureteral excess may undergo gangrene and slough flush with the bowel mucosa

sis due to the development of a fibrous nubbin (1 by 1 cm in diameter) at the orifice. Four months later the bowel was reopened, the nubbin removed, and a successful ureteroplasty performed. The postoperative pyelogram showed improvement (fig 5). The dog died 6 months later. At post-mortem examination the orifices were patent, the right ureter was dilated grade 2 and the kidney showed a recent infarct. In 4 dogs adequate fistulas were obtained. One died after 3 months due to localized peritonitis and a retained splenic mass. The remaining dogs were sacrificed after 7, 22 and 25 months.



FIG 3 Advanced bilateral ureterohydronephrosis (dog) 89 days after the sigmoidostomy resulting from ostial stenosis and excess ureteral projection of the lumen.

Dog No. 4 A large brown and white female had a two-stage ureteral anastomosis on September 23, 1947, and on October 28, 1947. The dog was entirely well. The follow-up blood urea nitrogen levels, however,

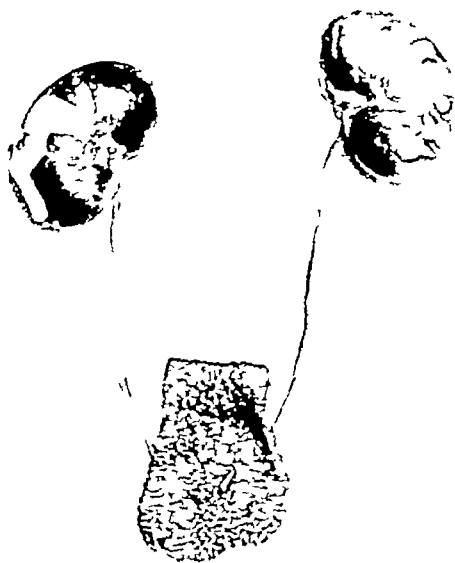
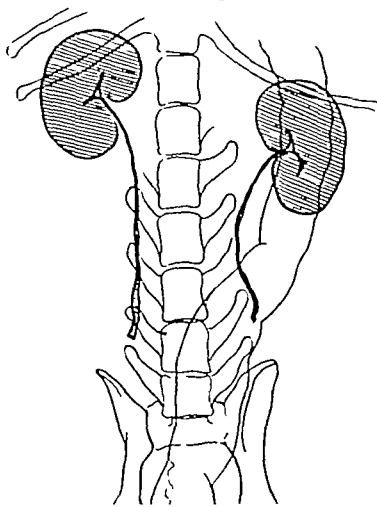


FIG 6 Dog No 4 Sacrificed 7 months after uretero intestinal anastomosis. Intact ureters and open bowel mucosal attachment. Free drainage, mucosal pyelonephritis were noted. Blood urea nitrogen values remained elevated.



Penicillin sulfonamides and streptomycin were administered postoperatively. The temperature became normal at the end of one week. The anterior portion of the wound healed by primary intention, the posterior half granulated in slowly urinary drainage from the wound was profuse at first but gradually lessened. Because of the persistence of a urinary loin fistula on the sixteenth postoperative day cystoscopy was performed and a 6F ureteral catheter passed to the renal pelvis without encountering any obstruction. It was left indwelling for 48 hours and following its removal, the wound remained dry. Follow up excretory urograms 6 months and 2 years later revealed a normal right renal pelvis and ureter (fig. 2).



FIG. 2. Excretory urogram 2 years after incision and drainage of loin for spontaneous perforation of ureter. Right kidney shows excellent function and normal pelvis and upper ureter.

DISCUSSION

Table I reveals that the sex is reported in 21 and the age in 19 cases. In considering these cases one finds that the incidence of rupture of the ureter with ureteral stone follows closely that of uncomplicated calculus. Thus, we find that the majority of the patients were in early adult life, although two were past sixty. While kidney and ureteral calculi occur with almost equal frequency in men and women, all but two of the cases in which extravasation have been found have been in men. The reason for this preponderance in males is not readily apparent. A study of the individual case reports reveals a history of previous major illness in only 4 of the 27 patients in this series. Two people had a previous prostatectomy, one benign prostatic hypertrophy 6 months and 10 years ago, one had a bilateral uretero-igmoal implant 15 years before because of exstrophy of the bladder, and the last had sustained a fractured spine and was bedridden for 6 months. Sixteen of the patients suffered no previous ureteral colic. The other eleven experienced renal colic ranging from several weeks to 8 years before the occurrence of further pain and extravasation. In two of them, however, the colic was on the contralateral side to the ruptured ureter. In this series, the right side was involved 15 times, the left 12. Although the average duration of symptoms in 21 cases prior to admission to the hospital was 12 days, the majority were between a few hours and one day. Two patients had been ill for 2 and 3 months respectively before coming under observation. The cases in this series revealed a complete absence of previous trauma. They had a clinical picture comprising the trilogy: 1) a sudden onset of pain at a site which occurred in all of the cases, 2) violent, deep, non-

tries were as follows

	1948	mg %
Blood urea nitrogen—January 23		46.3
February 20		35.0
May 29		39.0
Blood nonprotein nitrogen—August 11		42.0
August 25		41.5
October 21		38.1
February 11		41.4

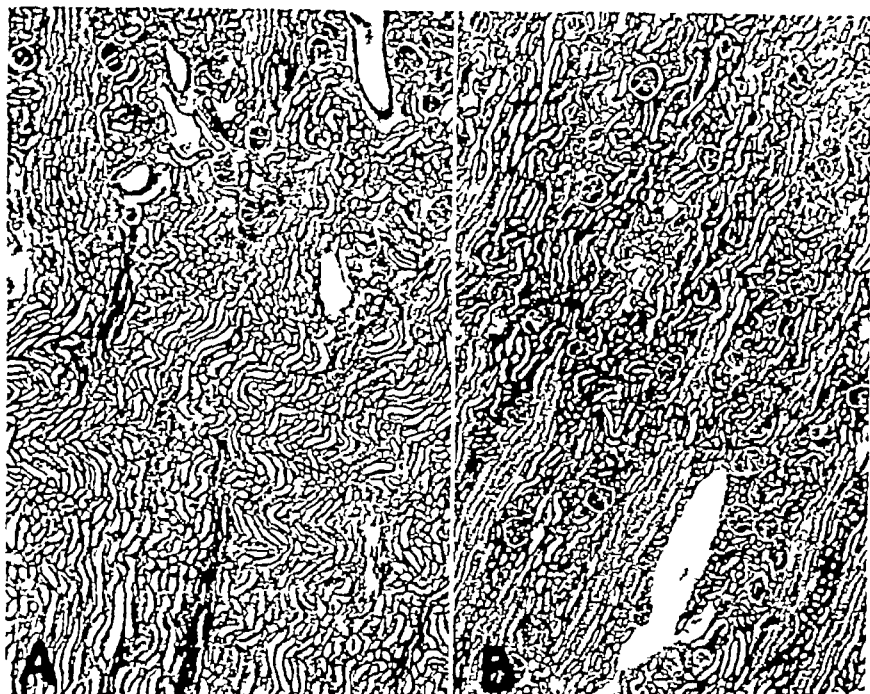


FIG. 9. Dog No. 7. A, right kidney normal 25 months after uretero colic anastomosis. B, normal left kidney 25 months after uretero colic anastomosis.

The postoperative excretory urograms were normal (fig. 8, 4). The ureters showed mild kinking above the anastomosis. On February 28, 1950, the dog was hydrated and adequate urine specimens for study were obtained. After 25 months the indigo carmine dye excretion was excellent in 5 minutes from the right and 6 minutes from the left catheter. The urine specimens showed many bacteria and an occasional pus cell on smear. The cultures showed a heavy mixed growth in each renal specimen. Microscopic section of the kidneys showed normal kidneys (fig. 9). The anastomoses showed an excellent mucosal bud of the orifices (fig. 8, B).

GROUP 3. SPATULA OPERATIONS WITH AND WITHOUT SPHINCTERS (fig. 2), 6 DOGS

In group 3 the spatula technique of the ureterocolic attachment was employed. The operations were carried out in one stage in 2 dogs and in two stages in 4 dogs. In the one stage operation both ureters were attached to the colon as

side in the two remaining cases. Cystoscopy was undertaken in twenty of the cases. A retrograde pyelogram was performed in seventeen and demonstrated extravasation in every instance. It was not done in 3 patients, in two because the urologist believed that the patient was too ill and in the other because of failure to visualize the ureteral orifice which was obstructed by a large middle prostatic lobe. No urine drained from the ureteral catheter in 11 cases, in four, obstruction was met at some point in the ureter. Indigo carmine injected intravenously in 9 patients revealed no excretion of the dye in 3 and poor excretion in 6. The belief that cystoscopy and retrograde study appear to be much more satisfactory for early and accurate diagnosis is borne out by the 20 cases in which this procedure was used. Retrograde pyelograms obtained in 17 not only helped to confirm the presence of the calculus when present, but resulted in excellent pyelograms indicating the localization and extent of the extravasation in every instance. No untoward results were seen to follow cystoscopy in these cases. The advantages to be obtained from such a procedure in establishing an early diagnosis far outweigh any possible hazards.

While nontraumatic extravasation of urine from the kidney always occurs in the organs in which there is antecedent pathological change such as infarct, hydronephrosis, polycystic disease, abscess or tuberculosis, pre-existing renal or ureteral disease is uncommon in spontaneous rupture of the ureter as in only one instance was an associated renal lesion discovered. This occurred in case 3, reported by Rathbun in which multiple perforations of the lower ureter at the site of a calculus were found coincidentally with tuberculosis of the corresponding kidney. On the other hand, this series of cases would seem to bear out the contention that spontaneous perforation of the ureter is almost invariably secondary to pyelo- or ureterolithiasis since a ureteral calculus could be demonstrated or recovered in 23 of the 27 patients. Although no calculus could be found in the case reported by me, the ragged perforation seen at operation, the finding of uric acid crystals in the urine with an elevated blood uric acid suggested the presence of a nonopaque calculus at some time. In some instances, raw areas in the ureter produced by the deposition of uric acid crystals or ulcerations brought about by previous cystoscopic ureteral dilatation might lead to actual perforation at a later date.

A review of the 23 cases in which a calculus could be found at the time of extravasation reveals that it was located within the ureter in 18 and outside the ureter in five. The position of the calculus within the ureter was upper ureteral in thirteen and lower ureteral in five. Nine of the upper ureteral calculi were located at the ureteropelvic junction while the other four were within 7 cm. of this region. The lower ureteral calculi were found within the lower five inches of the ureter. The calculus had escaped through the rent in the ureter and was found within a perireteral abscess in 5 cases; this abscess was low in 3 and high in 2. The site of the perforation in the ureter was found to be at or near the ureteropelvic junction in 20, lower ureteral in 3 and low lumbar in 1.

A study of the location of the calculus and the site of ureteral extravasation in the present series suggests that rupture of the ureter may take place by one of two meth-

Dog No 19 Large female, both ureters were attached to the colon intact during the first stage and anastomosed to lumen, second stage, by the spatula method on July 19, 1949 The dog remained entirely well The blood nonprotein nitrogen values were elevated on August 11, and August 25 54 and 43 mg per cent The dog was sacrificed on October 4, 1949 The ureters were not obstructed and the ureteral openings appeared adequate The right and left renal specimens revealed a heavy growth of mixed bacteria but contained only a few pus cells

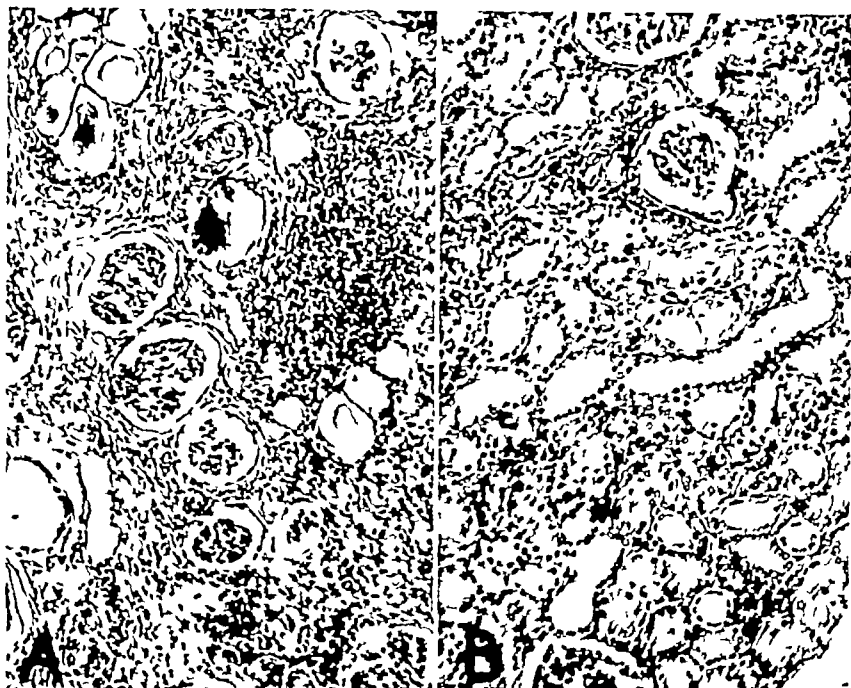


FIG 11 Dog No 17 A, left kidney Uretero intestinal anastomosis spatula without sphincter Diffuse lymphocytic infiltration fibrosis and acute chronic severe pyelonephritis B, right kidney Focal lymphocytic infiltration with slight tubular degeneration and chronic pyelonephritis

Bilateral spatula operations, left without and the right with a preliminary attachment Dog No 17 Female, medium size, was surgically prepared and during the first stage on February 7, 1949, the left ureter was transplanted by the Nesbit method and the right was attached intact During the second stage on March 8, 1949 the right ureter was anastomosed to the colon by the spatula method below the previous attachment The postoperative course was uneventful The blood nonprotein nitrogen on August 11, 1949 was 53.5 mg per cent and 68.1 mg per cent on August 25 Excretory urograms on July 14 1949 showed a mild left pyelo-ureterectasis (fig 10, A) and a normal right kidney and ureter On September 18 1949, the dog was sacrificed At this time the segment of the colon with the attached ureters was isolated and filled with skiodan solution A definite reflux was shown on the left and a slight trace on the right (fig 10, B) Post-mortem examination revealed adequate draining fistulas The left side showed

incision and drainage. The immediate postoperative course was uneventful. However, 1 month later the ureter re-ruptured at the site of the original perforation. Nephrectomy was then deemed advisable. Exploration in the third case revealed a large ureteral calculus in a markedly dilated ureter with multiple perforations and a large peri-ureteral abscess. Incision and drainage of the lower retroperitoneal area and section of the ureter was done as a preliminary procedure. Further investigation in this case revealed the presence of a tuberculous kidney which had undergone an autonephrectomy. Extirpation of the organ was performed at a later date.

Five patients were not subjected to open operative intervention. One patient was admitted in a moribund state. He was anuric and no investigation could be undertaken. Autopsy disclosed a perforation at the left ureteropelvic junction with extensive cellulitis of the retroperitoneal area. A second patient did not appear acutely ill and was observed without any cystoscopic manipulation while the remaining three in this group were subjected to repeated cystoscopy and dilatation of the involved ureter. These 4 cases had a good end result as the perforation healed in all without any distortion or stricture of the ureter.

The question of whether to cystoscope these patients pre- and postoperatively for the purpose of dilating the ureter was further reviewed. Two patients were treated with indwelling ureteral catheters to improve the function of the affected kidney, one soon after a diagnosis of extravasation was made and the other after a preliminary incision and drainage of the loin. Both were unsuccessful as nephrectomy eventually had to be done. Twelve cases are available for study of the fate of the ureteral calculus. Four patients were not operated upon. Three were cystoscoped and the ureters dilated. In each the calculus was extruded to the periureteral tissues. One was not cystoscoped and succeeded in spontaneously passing the calculus into the bladder. Of the 8 patients who were operated on, two were later dilated and succeeded in passing the calculus into the bladder. Of the 6 patients who were not dilated, all later passed the calculus, five into the bladder

Dog No 21 Female, weight 25 pounds, was surgically prepared and both ureters were transplanted into the colon on October 13, 1949, by a modified Nesbit method. This dog's convalescence was uneventful. The blood nonprotein nitrogen on December 28 was 46 mg per cent. On February 11, 1950, the non-protein nitrogen had risen to 106 mg per cent. Two days later the dog died suddenly and the post-mortem showed an acute suppurating bilateral pyelonephritis without ureteral obstruction (fig 14).

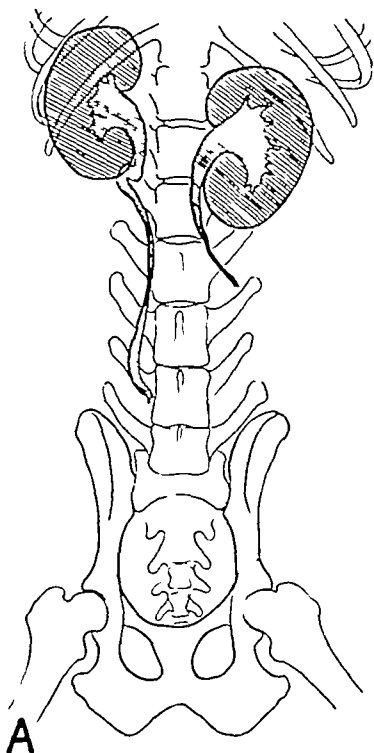


FIG 13 Dog No 20 ♀, bilateral spatula operation without sphincters on June 9, 1949. Pyelectasis, bilateral, grade 1. When dog was sacrificed 8 weeks after surgery, urine was cloudy, renal pelvis contained liquid feces. Nonprotein nitrogen blood values were 66.3 and 63.5 mg per cent 1 and 2 weeks before death. Microscopic sections showed acute pyelitis with little pyelonephritis. B, spatula transplant without sphincters. Liquid feces in each renal pelvis on post mortem examination. Acute pyelitis and minimal pyelonephritis 11 weeks after surgery.

The results of our spatula technique anastomoses were very interesting. Our best results were obtained where we utilized a preliminary trough attachment during the first stage in dogs 16 and 19. Poor results were obtained in dogs 20 and 21 when we utilized the spatula method without a protecting sphincter. In dogs 17 and 18 we wished to compare the results of the spatula anastomoses without a sphincter on the left and with a preliminary sphincter on the right.

CULTURES OF THE URINE

It is difficult to obtain accurate urine studies after both ureters have been transplanted into the colon. Our technique consisted of hydration, opening the

uncomplicated urinary calculus. They demonstrate a common trilogy consisting of sudden spontaneous-onset violent deep nonparoxysmic pain and intense prolonged contraction of the corresponding hemi-abdomen.

The diagnosis of spontaneous extravasation from the ureter may be difficult due to the fact that the presenting signs and symptoms in many of the cases point towards an intraperitoneal lesion. Cystoscopy and retrograde pyelography are more satisfactory than excretory urography for an early and accurate diagnosis. The localization and the extent of the extravasation were demonstrated in every instance where retrograde study was undertaken.

Once a diagnosis of extravasation from the ureter is established immediate exploration is indicated. The simplest procedure yielding the best results in the majority of the cases is incision and drainage of the lumen and/or the lower retroperitoneal area.

The seriousness of the problem of nontraumatic extravasation of the ureter is indicated by the fact that in this series 3 patients died and six others were subjected to nephrectomy either as a primary or secondary procedure. This was undoubtedly due to the delay in establishing a diagnosis and/or operating upon the patients or to sepsis and overwhelming infection of the retroperitoneal area. A review of this series also reveals that if the diagnosis is made early and incision and drainage done promptly the great majority of such treated patients will have excellent end results. It is also hoped that with this type of management and the more widespread use of the newer antibiotics that the results of a future series of such cases will surpass those reported in this paper.

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sults were as follows

	<i>Pus</i>		<i>Cultures</i>	
	<i>Right</i> 2-4	<i>Left</i> 2-4	<i>Right</i> Proteus	<i>Left</i> Proteus
Dog No 16, bilateral spatula with sphincters (2 stage)				E coli Aerogenes
Dog No 19 bilateral spatula with sphincters (2 stage)	1-3	1-3	Proteus E coli Streptococcus Clostridia	Proteus E coli Aerogenes Clostridia
Dog No 17, 2 stage spatula Right with sphincter Left without sphincter	occasional	+++	E coli	E coli Proteus Hem strep
Dog No 18, 2 stage spatula Right with sphincter Left without sphincter	1-3	+++	E coli	E coli Proteus Streptococcus Clostridia
Dog No 20, bilateral spatula without sphincters	++++	++++	Proteus* E coli Aerogenes	Proteus* E coli Aerogenes
Dog No 21, bilateral spatula without sphincters not cultured (died)			Severe pyelonephritis	

* Had liquid feces in each kidney

The urine examination following uretero-intestinal anastomoses suggests that all kidney urines become infected. Adequate drainage and absence of ureteral obstruction do not insure against postoperative infection. The establishment of a sphincter prior to ureterocolic attachment seems to minimize the number of pus cells and in some instances the number of bacteria. This was very decidedly shown in the urine examination of dogs Nos 17 and 18. The most severe infections were noted following bilateral spatula operations without protecting sphincters in dogs Nos 20 and 21. In both of these dogs the kidneys and/or pelvis showed acute infection.

BLOOD CHEMISTRIES

Ten of the 12 dogs in group 2 and 3 had blood urea or blood nonprotein nitrogen studies. It was of extreme interest to us that following bilateral ureterocolic attachment blood urea and nonprotein nitrogen clearances no longer reached normal control levels. In some dogs there seemed to be an immediate postoperative rise in blood urea but it would seek a lower level later providing adequate renal drainage was maintained. A typical example was seen in the blood chemistry studies in dog 7. Ten days after the uretero-intestinal anastomosis the blood urea nitrogen was 46.3 mg per cent. Two years later the nonprotein nitrogen was only 41.4 mg per cent. These readings suggest a metabolic disturbance due to reabsorption of catalytic substances. Tolerance to higher urea and nonprotein blood levels is developed and seemingly well tolerated providing free kidney drainage and minimal infection are maintained.

secured by interrupted sutures. He reported 6 operations on humans and 6 on dogs with only 1 mortality. In 1910 Rihmer, in experiments on dogs noted that an overlapping muscular tunnel often resulted in compression of the ureter. Martin in 1899 after much experimentation recommended bringing both ureters side by side through a 2.5 cm. muscular rectal canal and anchoring them about 1 inch below the bowel entrance. The ureters were closed over with muscular coats intended to aid the ureteral peristalsis.

In June 1918, Nesbit discussed the shortcomings of uretero-intestinal anastomoses and recommended a direct elliptical connection without the use of a sphincter. He believed that this new anastomosis would circumvent the most common anastomotic complications viz stricture formation at the anastomotic site, fibrosis of the ureteral stump projecting into the lumen of the bowel, and fibrosis from infection of the tunnel area. Operations have been performed upon dogs as well as humans and the postoperative results thus far have been uniformly excellent in every instance. Long time observations would be necessary to determine whether or not a valve-like oblique insertion through the wall of the bowel is a physiological necessity in protecting the upper urinary tract from dilatation and infection.

The direct anastomosis (axial method without suture of the mucosa to mucosa) was first tried by Glueck and Zeller in 1881. Both ureters were transplanted side by side through one stab rectal incision by Frank in 1898. He originated the anchoring suture to fix the end of the ureter. In 1932 Beaver and Mann reported on their direct implantation results with mucosa-to-mucosa sutures. In 37 cases in which axial transplantations were carried out there were 16 deaths, a mortality of 43 per cent. The dangers of direct anastomosis were pointed out by the peritonitis and stenosis of the ostium.

In April 1919 Cordonnier described a technique for a direct anastomosis of the ureter to the bowel without a tunnel, mucosa-to-mucosa application accomplished with minimal disturbances of the ureter. He reported successful results in 26 patients without mortality and a low incidence of complications and pyelonephritis (11 per cent).

Our experimental series of uretero-intestinal anastomoses in dogs can be divided into three groups:

Group 1. Two stage operation, an excess amount of ureter turned into the lumen of the bowel during the second stage (fig. 1, c).

Group 2. Two stage operation, the bowel opened during the second stage, and the mucosa of the ureter sutured accurately to the bowel mucosa (fig. 1).

Group 3. The spatula technique with and without sphincters (fig. 2).

Our dogs were surgically prepared and operated upon under intravenous anesthesia. Before the second stage (ureterocolic attachment) the dogs received 150,000 units of intramuscular penicillin and 1 gm. oral streptomycin. The colons were clamped and the abdomen shaved. Fine silk sutures were used to open the ureter and mucosa was attached to the bowel mucosa. For Group 1, the ureters were secured with 5.0 and 6.0 chromic catgut sutures on an atraumatic needle. All the anastomoses were replaced retroperitoneally. The abdomen was

sigmoidostomy on May 8, 1946. Prior to surgery cystoscopy revealed a normal bladder and ureteral transplantation was deferred. Between January 1947, and January 1949, three benign recurrences were treated transurethrally. On May 18, 1949, a suprapubic prostatectomy was performed. There have been no recurrences during the past year. At the age of 73 this man was probably spared the untoward effects of ureterosigmoidostomy and cystectomy.

A woman, aged 50, was examined recently who revealed a small, noninfiltrating papilloma of the bladder which was 1 cm. in diameter. She had no urinary symptoms. The bladder capacity was 16 ounces. A low grade infection was present and also residual urine which responded to surgical treatment. She had been advised to have an immediate total cystectomy. One cannot help but wonder whether or not a radical procedure at that time was indicated.

There is now a sharp difference of opinion whether or not a bowel tunnel is necessary when the ureters are transplanted into the colon. Nesbit and also Cordonnier have counselled against the use of a tunnel. Nesbit advised an oblique and Cordonnier a direct attachment without a tunnel. Only time can evaluate this new concept. All previously reported ureterocolic anastomoses without protecting tunnels have resulted in failure.

The spatula technique of ureterocolic attachment will result in a permanent functioning fistula. We have noted that there is a marked shrinkage of the original opening but the mucosal bud is preserved (fig 15, *B*). Even without obstruction, varying degrees of infection will gradually reduce the renal reserve. Loss of renal reserve may be manifested by elevation of the blood nitrogen, changes in blood pressure, high grade secondary anemia, low grade fever, and general feeling of ill health and inanition. This under par physical status may be accompanied by a peculiar uremia-like body odor. Ferris and Odel in a recent excellent paper discussed blood electrolyte patterns in 141 patients who had undergone bilateral ureterosigmoidostomy. They found a hyperchloremia and acidosis in 80 per cent of their postoperative patients. In addition they found these disturbed electrolyte patterns were reversible with appropriate diets and soda bicarbonate administration.

It is believed that the spatula technique is followed by minimal postoperative reactions. All of our present experiences indicate that renal contamination, infection and reflux may follow these ureteral transplants. The following case report is of interest.

R. C., aged 59, was admitted to Passavant Memorial Hospital, July 29, 1949, with a large carcinoma of the prostate, urinary retention and obstipation. Excretory urograms showed bilateral hydronephroses, grade 2 (fig 16). The blood count was low and the blood urea nitrogen was 20 mg. per cent per hundred cubic centimeters of blood. The blood acid phosphatase showed 2 units. Cystoscopy and biopsy suggested invasion of the carcinoma into the bladder neck. Bilateral spatula ureterosigmoidostomy without sphincters was carried out on August 12. The operation was followed by daily fever (99 to 101F), abdominal distention, epididymitis and mild right thrombophlebitis. The patient was discharged on September 1. The blood count was now 4.01 red blood corpuscles,

thereby minimizing stenosis of the new ostium. In the 3 dogs where the excess ureters were left in the bowel lumen, bilateral ureterohydronephrosis and renal insufficiency followed constricted orifices after 6 weeks, 2 months and 3 months (fig. 3).



FIG. 2. Two stage spatula anastomosis. Intact ureters laid into bowel trough during first stage and replaced retroperitoneally. *a*, Distal ureter divided. *b*, Bowel fistula made. *c*, Ureter spatula carefully prepared. *d*, Ureteral and bowel mucosa accurately anastomosed with continuous 00000 chromic locked sutures. *e*, Second row of interrupted 00000 chromic sutures joining adventitia to serosa. *f*, Anastomosis replaced retroperitoneally.

GROUP 2. TWO STAGE OPERATION. THE BOWEL OPENED DURING SECOND STAGE (fig. 1), 6 DOGS

The 6 dogs in group 2 were operated upon in 2 stages. During the first stage the intact ureters were anastomosed to the colon through a small bowel trough (fig. 1). No complications followed the first stage. During the second stage both ureters were divided 2½ cm. below the anastomoses. The free ends were now turned into the bowel lumen through a small stab wound just where they egressed from their attachment. Following this procedure the colon was opened, the excess ureter resected and the mucosa of the ureter carefully sutured to the bowel mucosa with 4 fine 5/0 or 6/0 chromic gut sutures (fig. 1, *f*). Four of the 6 dogs obtained satisfactory functioning fistulas and mucosal buds. In 1 dog calculi and excoelentera developed. Dog 3 developed a unilateral hydronephro-

ing the ureter elsewhere. In advanced cases of renal destruction diversion of the urine from the bowel may be necessary to prevent renal insufficiency. The following case seems to illustrate the discouraging results which may follow some of our ureterocolic attachments.

The case of L. Z., aged 21, was previously reported in 1942. A two stage anastomosis of a single ureter was carried out in 1938 for bladder exstrophy. Post-



FIG 16 R. C., male aged 59, admitted July 28, 1949 for acute retention, large carcinoma of prostate and bilateral hydronephrosis. Bilateral ureteral transplants on August 12, spatula technique without sphincters. Blood count, September 1: red blood corpuscles 4,011, hemoglobin 7.9 gm., white blood corpuscles 10,850. Fever chart depicted. Acid phosphatase 2.05, protein 7.31 gm., and carbon dioxide 14.6 miliequivalents. Prior to retroperitoneal prostatectomy and cystectomy, temperature controlled by penicillin and dihydrostreptomycin.

operative obstruction was relieved in 1940 by nephrostomy and rectal destruction of a granuloma. Recurrent ureterocolic obstruction of the right ureter occurred in 1949. The blood showed a moderate anemia and the blood urea nitrogen was 56 mg. per cent. The phenolsulfonphthalein output was 5 per cent in 2 hours. A nephrostomy tube was inserted on August 10, 1949. The urine showed marked pyuria and B. proteo-aerogenus. The nephrostomy was followed by marked improvement (fig. 17) and the blood urea nitrogen fell to 19.6 mg. per cent on November 7. On November 16, 1949, the abdomen and colon were opened and a granuloma was resected from the ostium. In addition, a meatotomy was done. The post-operative course was uneventful. The nephrostomy tube was removed 12 days

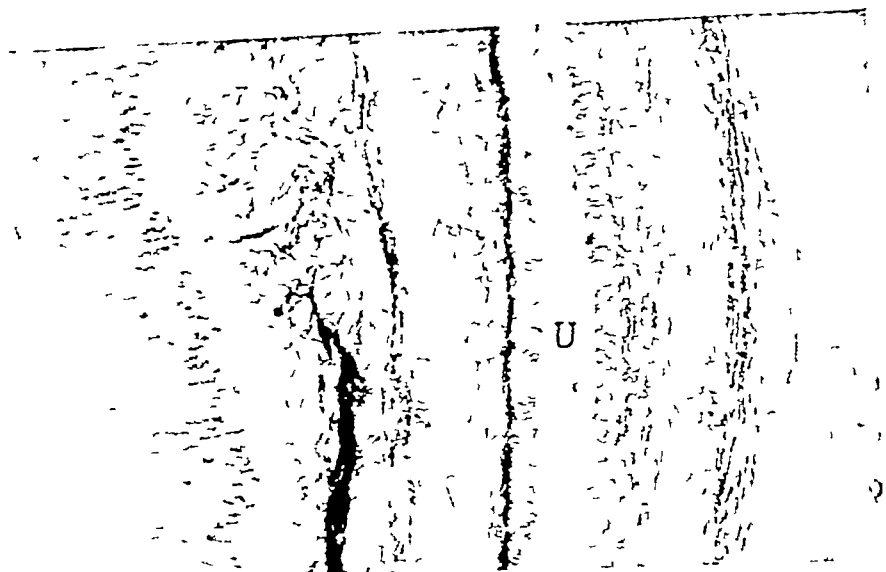


FIG. 4. Complete absence of inflammatory reaction following first stage transplantation of an intact ureter into colon wall.

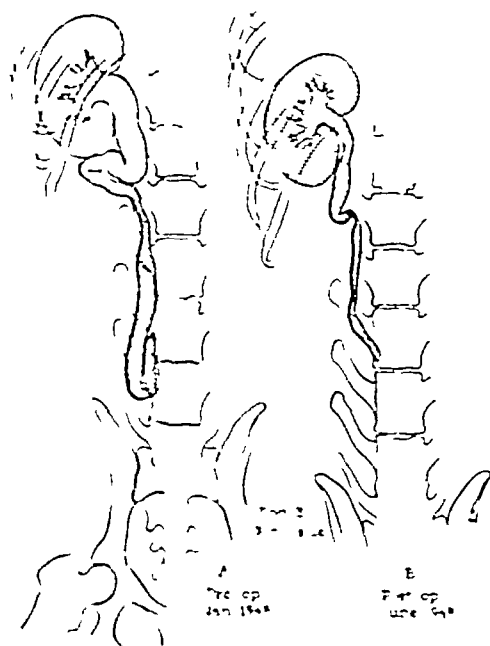


FIG. 5. D.K.N. 10 months after ureterocolic anastomosis (fig. 1): right ureter be-
cause of a fibrous nubbin occluding ostium was found. On February
10, 1948, the right ureter was successfully removed followed by generous meat
excision. The patient showed marked improvement. From January to May 1948
the blood urea nitrogen was 32, 31.0 and 27.5 mg. percent per 100 cc blood.

dilatation of the ureter or obstruction (fig. 6). The kidney sections
showed no evidence of obstruction. The mucosa showed mucosal buds.



FIG. 18 L Z Right kidney. Acute and chronic pyelonephritis, marked



FIG. 19 Single ureter transplanted for exstrophy in 1938. Ostial obstruction successfully relieved by rectum in 1949. Recurrent obstruction successfully relieved through open bowel in 1949. Patient died 6 weeks after abdominal ureteroplasty of acute renal failure following upper respiratory infection. Post mortem specimen revealed no ureteral obstruction. Microscopic sections showed severe acute and chronic pyelonephritis.

Dog No 6 A large black and white female had a two-stage uretero-colic anastomosis on December 9 1947 and on January 6 1948 The dog remained entirely well and gained 10 pounds in weight Excretory urograms taken March

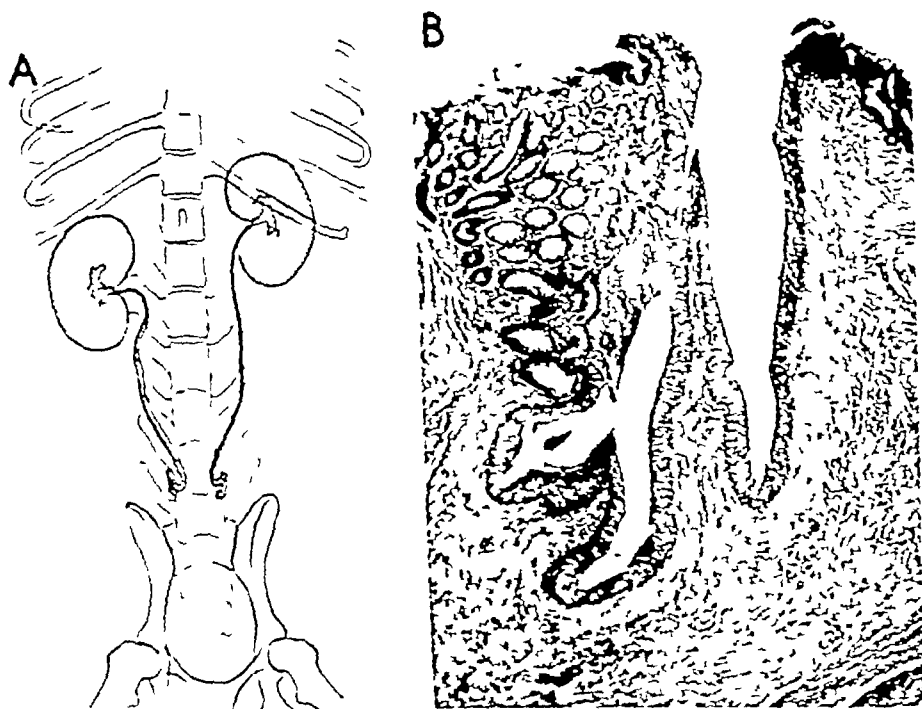


FIG. 8. Dog No 7. A, bilateral two-stage ureteral transplantation, intact ureters and open bowel anastomosis. Pyelo ureterograms remained normal after 25 months. On post-operative examination urine showed heavy mixed bacterial growth on culture but no pus. B, post function excellent. Microscopic sections of kidney showed minimal pyelonephritis. B, ureterointestinal anastomosis mucosal bud functioning perfectly 25 months after operation. Mucosa of bowel and ureter have remained approximated without intervening scar tissue. (Whitlock)

1948 were normal (fig. 7). The post-operative chemistry findings were

		BUN
Blood urea nitrogen	January 23	32.5
	February 20	33.3
	May 20	37.8
Nephrotic nitrogen	August 11	54.0
	August 25	47.0
	October 21	46.0

The dog died suddenly on October 26 1949 twenty-two months after surgery. The catemetic blood chemistry values remained persistently elevated. At a delayed post-mortem examination we could determine only that there was adequate blood flow without obstruction.

Dog No 7 Undergoes two-stage ureteral transplantation on December 17 1947 and January 15 1948. The dog remained entirely well. The blood chemis-

necessary. Our experience leads us to believe that the spatula operation without tunnels is apt to be followed by more renal contamination, reflux and infection. All ureterocolic attachments reveal varying degrees of infection. The infections remain minimal in the presence of good drainage and a flexible compressible ureterocolic tunnel.

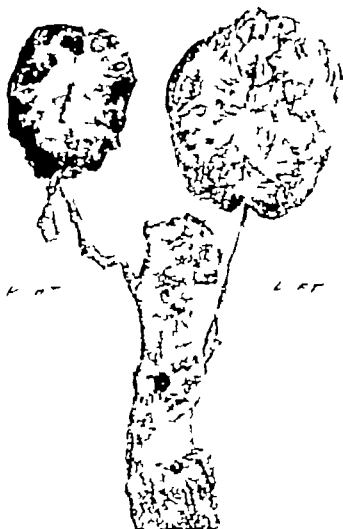


FIG 21 No ureteral obstruction 12 years after three-stage ureterosigmoidostomy. Ostia patent and showed mucosal bud. Right kidney small and both appeared granular. Microscopic sections showed advanced arteriosclerosis and pyelonephritis.



FIG 22

Reflecting upon our past experiences one may well wonder whether or not the ureters should be routinely transplanted into the colon. There are profound constitutional disturbances of varying degrees initiated as soon as both ureters are transplanted into the colon. These disturbances result from reabsorption of waste and electrolytic substances. Varying degrees of postoperative renal infec-

recommended by Nesbit. We, however, used 2 rows of sutures the first layer opposed the ureteral and bowel mucosa while the second interrupted 5-0 chromic catgut sutured the adventitia to the serosa. In 2 dogs only the left ureter was attached to the bowel by the Nesbit method while a mobilized portion of the right ureter was transplanted intact into a trough made in the adjacent colon. During the second stage the right ureter was divided and attached to the colon below the sphincter by the spatula technique. In the remaining 2 dogs both ureters were transplanted intact during the first stage. During the second stage the ureters were attached to the colon below the sphincters by the spatula method.



FIG. 10. Dog No. 17. A, bilateral spatula anastomosis, right with tunnel and left without. B, 1 ft. colon showed advanced pyelonephritis, pyelo-ureterectasis and calculi. Right kidney still free of bacterial infection. B, shadow in 30 cc injected into isolated colon segment containing ureteral attachments. Left ad. showed reflux of dye with only trace on right.

Bilateral spatula operations with preliminary intact ureteral attachment. Dog 16, female, pregnant, medium size, was operated upon in two stages on January 25, and May 3, 1949. During the first stage both ureters were attached intact to the colon. During the second stage both ureters were anastomosed below the previous attachment with the spatula technique. The dog remained well even though the nonprotein nitrogen values were elevated to 51.6 and 58.0 mg. per cent 4 months later. Excretory urograms showed mild bilateral pyelo-ureterectasis (fig. 11). The urine specimen from right kidney showed 2-4 pus cells per high power field and B. proteus on culture. The left specimen showed 2-4 B. proteus and 1 B. proteus, coli and aerogenes on culture. The dog was sacrificed on December 9, 1949. The ureteral orifices were adequate and patent. Autopsy on colon and ureters revealed no reflux.

The operation should not be recommended unless a strong indication exists. Treatments other than total cystectomy may finally improve our late end results.

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advanced pyelonephritis (fig 11, A), pyelo-ureterectasis and calculi. The right kidney showed a low grade infection (fig 11, B).

Dog No 18. The ureters were transplanted in 2 stages—February 12, and May 24, 1949. The left ureter was transplanted without a sphincter by the spatula method and the right ureter with a preliminary attachment and sphincter. This dog remained very active and well until she was sacrificed on September 20, 1949. The nonprotein nitrogen values on August 11 were 51.8 mg per cent and 48 mg per cent 2 weeks later. Excretory urograms on July 19 suggested a mild stenosis of the right orifice, otherwise normal (fig 12). The post-mortem

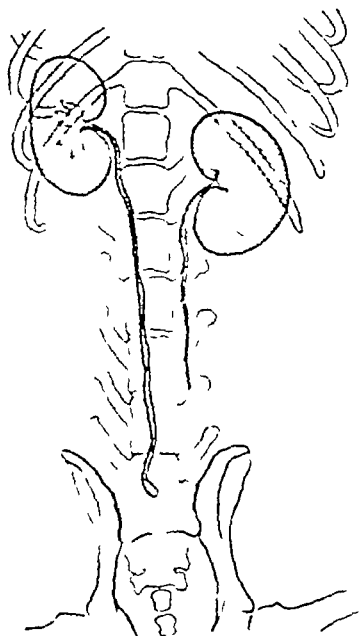


FIG. 12. Dog No 18. Right spatula with sphincter, left spatula without sphincter. Urine from right kidney showed occasional white blood corpuscles and heavy growth of *E. coli*. Left urine showed many pus cells and heavy growth of mixed bacteria. Mild right ureter ectasia. Slight kinking of left ureter above anastomosis at post-mortem examination.

findings, however, revealed adequate ureteral openings. The left lower ureter was slightly kinked which may have prevented antemortem ureteral reflux.

Bilateral pyeloplasties without sphincters. Dog No 20. Female, weight 30 pounds, was surgically prepared and both ureters were transplanted by a modified No. 10 method on June 7, 1949. The dog began to lose weight immediately after the operation and required 2 weeks antibiotic therapy before she again could eat satisfactorily. Excretory urograms made on July 12, 1949, showed bilateral pyelectasis (fig. 13, A). The nonprotein nitrogen blood value on August 11, 1949, was 63 mg. and 63.5 mg. per cent on August 25. The dog was sacrificed on August 30, 1949, and post-mortem examination showed liquid feces in the rectal pelvis. The right ureter and pelvis were dilated grade 4. The ureters were completely obstructed. The microscopic sections of the kidneys showed acute pyelitis and minimal bilateral pyelonephritis (fig. 13, B).

were dysuria, urgency and frequency. He voided a good stream, and had no difficulty in starting the flow. There was no residual urine. In the past, his health had been good with the exception of a chest injury several years previously, which had necessitated some minor surgery. His family history was negative for tumor.



FIGURE 1

On physical examination the pupils reacted to light and distance. The heart, lungs, and abdomen showed no abnormalities. On rectal examination the prostate was moderate in size, not tender, and of normal consistency. The external genitalia were normal. The reflexes were normal. The electrocardiogram was normal for the patient's age. On cystoscopy no ulcer or stones were present. The ureteral orifices were normal in position and appearance. On the left lateral superior wall of the bladder, above the orifice, was a large greyish-white, smooth tumor.

abdomen and puncturing the ureters with an appropriate sized needle above the anastomoses. In this way adequate specimens could be obtained for study. In dog No. 7 the ureters were catheterized through a small ureteral incision above the attachments.

One dog in group 2, and 5 dogs in group 3 had urinalyses made before death. *Group 2 (one dog), two stage operation, second stage open bowel (fig 1)* Dog No. 7 was sacrificed 25 months after operation. The specimens were collected

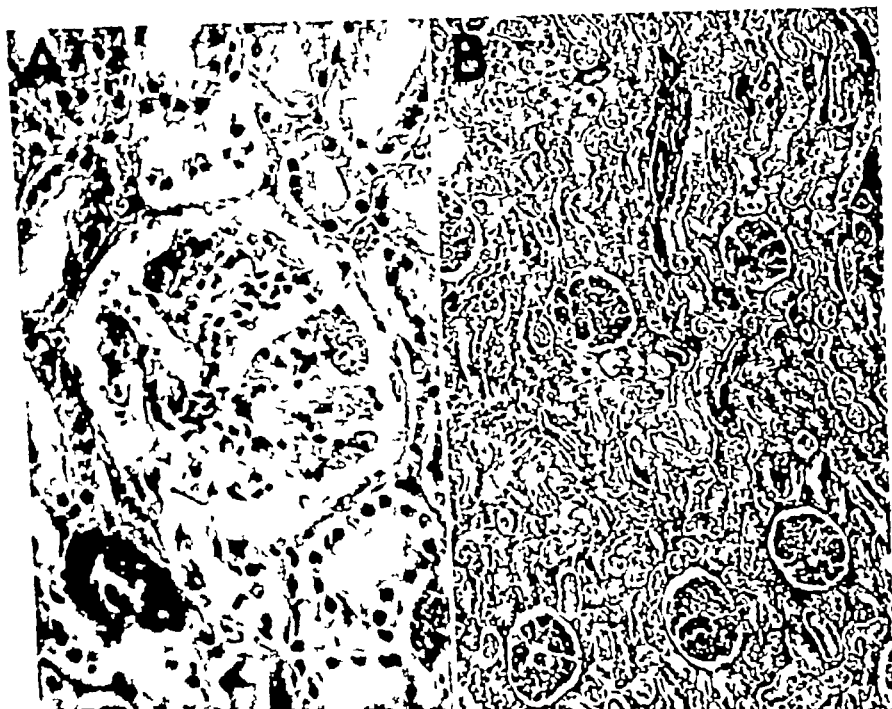


FIG. 11. Dog No. 21. *A* invasion of kidney by gas forming bacilli (Clostridia) through ureters from colon. Bacilli seen in glomeruli and interstitial tissues. *B* left kidney. Diffuse tubular degeneration and interstitial edema in clostridial infected kidney.

with catheters passed through a small ureteral incision. Adequate renal specimens were obtained for study. At the same time renal functions were determined with intravenous indigo carmine.

Time	Culture	Kidney Function
Right	0.2	5 min. excellent
	Proteus	concentration
	Aerogenes	
Left	0.2	6 min. excellent
	Proteus	concentration
	Aerogenes	

In dog No. 7 twenty-five months after surgery the kidneys were draining adequately and the renal function was excellent. There was no ureteral stenosis and the microscopic kidney sections showed no inflammatory changes. The culture, however, showed a high grade bacilluria without pus. The new ostia to the cyst mucosa had (fig. 8, B).

Group 3. Single operation with and without splenectomy. In this group the re-

Urine protein, positive, sugar, negative, red blood cells, negative, white blood cells, 4 plus, casts, negative, crystals, negative, culture and stain, negative

Operation was performed at St. Anthony's Hospital on June 9, 1948. A suprapubic cystotomy was done and a large, smooth, firm tumor on a short pedicle about 1 cm in length with a base 1 cm in diameter was found attached to the left lateral posterior superior wall of the bladder above the trigone. The tumor was approximately 10 cm in diameter, mushroom shaped, and 4 to 6 cm in thickness. It was severed with a cutting current and the bladder base fulgurated.

The following is the tissue report by Dr. B. Portuondo. The specimen consists of an ovoid tumor which, has the shape of the top of a mushroom (fig. 1). It measured 10.6 by 9.4 by 5.7 cm and weighed 137.7 gm. The surface contained one irregular bulge on one side, and was thin, shiny and of a silvery-white color throughout. There was an excavation on the underside in the central portion, which was the site of the pedicle attachment. The cut surface showed a homogeneous, smooth, firm, apparently fibrillary shiny appearance.

Sections showed, in some areas, intact transitional cell epithelium and in others coagulative necrosis densely infiltrated with various leukocytes, especially neutrophils, plasma cells and lymphocytes. The tumor, as a whole, was composed of bundles, which in some areas were quite fibrillary and in others cellular. These bundles were composed of fibrillary eosinophilic staining material with basophilic staining nuclei, most of which were elongated and spindle-shaped tapering more to a point on one end than on the other. Mitotic figures were present but infrequent. This tumor would appear to be a cellular fibroma arising from the wall of the bladder.

The patient left the hospital July 9, 1948, dry suprapubically, with a good bladder capacity, and voiding a good stream.

1115 Paul Brown Bldg., St. Louis, Mo.

Ureterocolic anastomoses are more difficult to perform in dogs than in humans. Following poorly functioning anastomoses a dog will usually not survive longer than 3 to 4 months. Poor drainage usually results from stenosis of the orifice and severe infection. Every transplantation of ureters into the colon is followed by some degree of infection. When the new ostium remains permanently patent the infection may be only a bacilluria. Antibiotics and or chemotherapy will reduce and minimize the degree of infection following surgery. Pyuria and reflux were more evident in dogs where the anastomoses were performed without preliminary attachments. The blood chemistries continued to show persistent elevation following surgery. Reabsorption of excretory products from the colon predisposes to disturbed postoperative blood chemistries. The highest chemistry levels were noted in dogs following ureteral transplants without previous attachments. We obtained our best results in dogs following the 2 stage operation. Bilateral preliminary attachment of the intact ureters to adjacent bowel troughs allows healing by primary union without infection (fig. 4). Accurately suturing the ureteral mucosa to the bowel mucosa through an opened colon will result in a more permanent mucosal functioning ostium. The same mucosa-to-mucosa attachment and a permanent functioning fistula can now be obtained by the spatula operation of Nesbit. The spatula operation in dogs without preliminary bowel attachment can result in fecal renal contamination, reflux, severe infections and renal insufficiency. Our experimental evidence indicates that the bowel tunnel may be just as important to the transplanted ureter as it is in a normal bladder and ureter. Postoperative contamination or infection of the urinary tract by the bowel bacterial flora is exceedingly common. These complications seem to be more severe when the kidneys are unprotected by a tunnel or sphincter.

Our improved knowledge in this field of surgery and the intelligent use of antibiotics and chemotherapy are resulting in better ureteral transplant operations and permanent functioning fistulas. Many untoward postoperative features, however, are still overlooked by the average surgeon. The enthusiasm and desire for a large series of cystectomy cases could include patients who might have been treated preferably by conservative methods. A patient may become chronically ill after the ureters are anastomosed to the colon. Smith recently commented upon the poor results and the small number of survivals following ureterocolic anastomoses and cystectomy for malignancies. He also noted the superior result when the surgery was carried out for benign lesions. The supreme caution that should be exercised by the surgeon in recommending cystectomies is exemplified by the following case report:

first comprehensive review on the subject. Since then, Kellogg,² Higgins,³ and Peters⁴ have published outstanding contributions.

More specifically on fistulas caused by foreign bodies, Fowler⁵ has compiled a classification from the literature. Most foreign bodies in the bladder reach there through the urethra. They may also reach there from the ureters, penetrating wounds and injuries and by migration from adjacent structures. In a series of 36 cases of migrating foreign bodies, collected by Monarschkin in 1926, only five had perforated the bowel.⁹

In 1936, Herbst and Miller,¹⁰ in an excellent review, point out that it is difficult to cull out these cases because it was not specifically stated whether the foreign body had been ingested or had been introduced into the bladder. Specific cases where foreign bodies entered the bladder other than through the urethra are as follows. Kingdon¹¹ in 1842 reported fistula due to a needle passing from the appendix into the bladder. Roberts¹² reported a case of bladder stone formed from a slate pencil ingested 6 months previously. A case of an elderly physician is mentioned who after 9 years of pneumaturia and fecaluria passed a partridge bone per urethram. Harrison¹³ reported a case of fistula caused by an ingested rabbit femur. Pins have been the most common foreign body producing fistula.⁴ Wooden splinters, crochet needles, and ingested bullets have also been reported.¹¹ Herbst¹⁰ reported a chicken bone and Baron¹⁴ a whiskbroom bristle. Migratory bodies such as shell fragments,¹³ needles, Kirschner wires,¹⁵ bullets,¹⁶ etc., have been reported.

Our case is believed to be the first recorded instance of intestino-vesical fistula due to an ingested partial dental plate.

Intestino-vesical fistula occurs more often in the male, 3:1. This is said to be due to the fact that diverticulitis is more common in the male and that the uterus in the female acts as an anatomical barrier between the bowel and bladder.^{2, 4, 5, 6}

Traumatic, congenital and neoplastic fistulas have obvious explanation for their formation.

Appendiculovesical fistulas depend on an appendiceal abscess burrowing into the bladder or upon a very long pelvic appendix with subsequent appendicitis and adherence to the bladder.¹⁷

In cases of diverticulitis, developing fistulas, fecal material and bacteria fill a diverticulum. An acute inflammatory reaction develops, the opening into the bowel is closed off, peridiverticulitis occurs with formation of dense adhesions between the bladder and bowel. The inflammation may subside or suppuration may occur followed by the development of a fistula between the two organs.^{3, 6}

Ingested foreign bodies form a fistula by impinging on a transverse fold of the

⁹ Monarschkin. Quoted by Fowler, H. A., in *Tr. Am. A. Genito-Urin. Surg.*, **25**, 297-311, 1932.

¹⁰ Herbst, R. H. and Miller, L. M. *J. A. M. A.*, **106**, 2125-2128, 1936.

¹¹ Penhallow, D. H. *Ann. Surg.*, **95**, 792-794, 1932.

¹² Baron, S. and Lipshutz, H. *J. Urol.*, **55**, 358-362, 1946.

¹³ Lattimer, J. K. *J. Urol.*, **55**, 483-485, 1946.

¹⁴ Bors, L. and Bowie, C. F. *J. Urol.*, **55**, 358-362, 1946.

¹⁵ Branham, D. W. and Richey, H. M. *J. Urol.*, **57**, 869, 1947.

¹⁶ Wilker, A. S. and Kaufman, D. R. *Urol. and Cutan. Rev.*, **46**, 217-219, 1942.

¹⁷ Meisel, H. J., Kagan, H. N. and Miller, J. M. *J. Urol.*, **61**, 43-45, 1949.

and 12.5 gm hemoglobin. He was re-admitted on October 16, 1949. The blood count had dropped to 2,96 red blood corpuscles, 7.9 gm of hemoglobin, and white blood corpuscles 10,800. The blood urea nitrogen was 12 mg per cent, and the total proteins 7.31 gm. The blood acid phosphatase remained at 2 units. The sedimentation rate was 50 mm and there was a daily fever of 98 to 103°F.

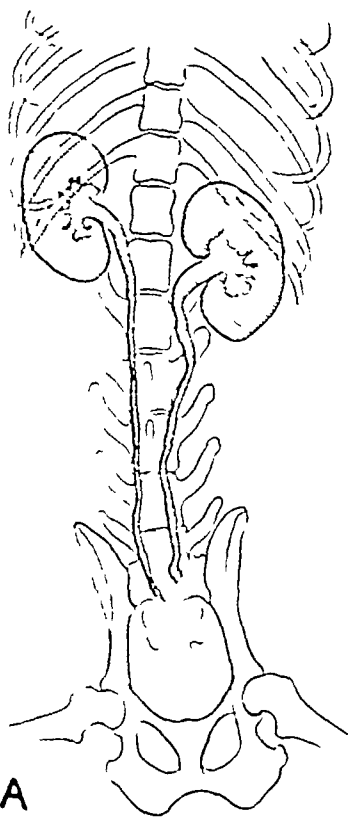


FIG. 1. Dog No. 16-1, two stage bilateral spatula ureterocolic operation following colonic intact ureteral bowel attachment. Bilateral mild ureterectasis. New orifices patent, no demonstrable ureteral obstruction. Nonprotein nitrogen blood values elevated to 6.0 mg per cent. B, ureterocolic anastomosis, spatula technique with sphincter, 10 mm. Mucosal blood preserved. Orifice has shrunk from 12 mm. to 4 mm. in diameter.

Fig. 1B. One gram of dihydrostreptomycin and 100,000 units of penicillin were initiated daily on October 25. He became afebrile and a radical retropubic prostatectomy and cystectomy were done on October 28. The patient made a satisfactory hospital recovery and was discharged to his home on November 5, 1949. Two weeks after returning home he died suddenly. The surgical specimen (prostate and bladder) suggested that the prostatic carcinoma had been entirely removed.

When the ureters become obstructed after ureterosigmoidostomy, the tendency is to procrastinate too long before an effort is made to relieve the obstruction. In such cases a nephrostomy tube may be life saving. Later it may be possible to relieve the obstructed anastomoses by opening the colon or reimplant-

barium enema is to outline the bowel and give a clue as to the etiology of the fistula. Far better in some instances, is the use of dilute diodrast which by its low viscosity passes readily from bowel to bladder or vice versa and gives an important clue. Sodium iodide is too toxic if absorbed in large quantities and should not be used.

As stated previously, it may be impossible to visualize the tract except at surgery. At any rate, it is always important to harbor a high index of suspicion in persistent urinary infections with bizarre odors and flora. Also in cases where known bowel disturbances have been associated with vesical symptoms, one should be suspicious.

The therapy in foreign body fistula is primarily surgical.^{2 4 5 6 7} Heretofore, surgery was performed in stages with preliminary colostomy as the first step. Occasionally, the operation was completed in one step. This was the exception, however. Today, armed with modern surgical methods and aided by bowel sterilization with sulfonamides and antibiotics, this is all done in one stage, the fistula being excised and the rent in the bladder and bowel sutured.¹

This is primarily a procedure for the general surgeon⁷ as the vesical component requires little more than suture of the defect and an indwelling urethral catheter for about five days.

The prognosis in this type of case is excellent.

CASE REPORT

A H, No A-85584, a 52 year old single white male grill proprietor, was admitted January 30, 1949, complaining of pneumaturia for 2 months and fecaluria for 1 month.

Eight months before admission, he lost his partial upper dental plate while on a drinking spree. He was certain he had swallowed it but was reassured by his cronies that he must have misplaced it. A thorough search having failed to locate it, he visited a physician who fluoroscoped him and found nothing.

He was asymptomatic until 2 months prior to admission when he noticed gas and air coming out of his urethra either during the act of micturition or at the end. One month prior to admission, he passed fecal material per urethram. During the past month, he developed urgency and frequency, 10-12 times, but usually passed very small quantities of urine, often fecally contaminated. Occasionally, bright red blood passed in the urine. Urine was not passed per rectum and there was no unusual change in bowel habits. There was a 15 pound weight loss in 6 months.

Past history revealed life-long bronchial asthma and hayfever. A minor nasal operation had been performed. He suffered from chronic dyspnea and imbibed frequently to excess with poor food intake and frequency and hematuria during alcoholic sprees. The family history and review of systems revealed nothing.

Physical examination revealed a poorly nourished white male, chronically dyspneic. The dyspnea was uninfluenced by position. There was mild cyanosis of nail beds and lips. There was moderate obstruction of the right nares. Chest and lungs revealed the characteristic findings of emphysema and chronic bronchial asthma. The heart and abdomen were normal. The genitalia were normal and the prostate was small and fibrotic.

¹ Ormond, J. K. J. Urol. 61: 554-556, 1949.

after the abdominal surgery and patient was discharged on December 4. After being at home for 10 days she had an acute sore throat. The infection precipitated an acute uremia. Re-admission on December 14 showed the blood urea nitrogen 76 mg. per cent, carbon dioxide combining power 5.3 milliequivalents (24-30 normal), blood chlorides 113 milliequivalents (99-108 normal). The blood count has dropped to 2.9 red blood corpuscles and 7.5 gm. hemoglobin. The tube was re-inserted but no retention of urine was noted. Medical treatment brought the C₀ combining power up to 24 milliequivalents and chlorides down to 107 milli-



Fig. 17, L. Z. and 21. Single kidney. Preoperative excretory urograms showed right ureter hydronephrosis. Ten days after nephrostomy tube insertion marked clinical and radiographic improvement.

equivalents. She expired on Christmas day and the post-mortem showed severe acute and chronic pyelonephritis (fig. 18), uretero-pylectasis but no demonstrable obstruction (fig. 19).

It appeared to us that we should have allowed the nephrostomy tube to remain longer or re-implanted the ureter elsewhere. The colon epithelium showed no change or metaplasia after 11 years. In spite of the good drainage which had been established the patient succumbed to acute renal insufficiency. This was precipitated by an acute infection superimposed upon a chronic pyelonephritis.

Many surgeons, after the ureters have been successfully transplanted, tend to ignore the necessity of postoperative care. It is in these follow-up studies that some of the shortcomings of ureterocolic anastomoses are uncovered. Most of these patients have blood disturbances, varying degrees of infection, and vascular changes. Even adequate drainage does not insure the patient against the

fifth postoperative day and the patient voided normally with clear urine. He was discharged on the ninth postoperative day.

There has been no recurrence of symptoms to date.

DISCUSSION

Often it is difficult to state whether a foreign body in the bladder has been ingested or entered the bladder by way of the urethra. The mechanics of formation of the fistula in certain instances will close the fistulous communication behind the advancing object. As the object enters the bladder it will frequently be attached to the bladder at its point of entry or a white scarred ureter will be observed in the bladder wall. Conversely, a foreign body entering the bladder through the urethra may frequently form a calculus and roll about free in the bladder without a point of attachment or of scarring.

Cases seen in routine practice in the absence of obstructive uropathy, with persistent cystitis and recurrent urinary infection must be suspected of fistulous communication or of foreign body.

There is no routine program to follow in establishing the diagnosis. The history and cystoscopy are the two most valuable aids.

In the case presented, it is amazing that such an object with hooked projections at each end could progress so far before being arrested in its passage.

SUMMARY

A unique case of intestino-vesical fistula due to a swallowed partial plate is presented.

The literature has been reviewed.

Mechanisms in the formation of various types of fistulas have been presented and the clinical and diagnostic features have been discussed.

75 Willett St., Albany, N. Y.

development of irrevers-ible deleterious changes. That point is well illustrated by the following case history.

O. C. aged 60 had a three stage ureterocolic anastomosis for a benign lesion in 1938. She enjoyed reasonably good health until 1948. In November 1949, excretory urograms showed a small right kidney, a large left kidney with no obstruction but poor visualization. The blood urea nitrogen was 45 mg. per cent. The blood pressure was 200/104. In January 1950 the blood urea nitrogen was 55 mg. per cent and she expired in uremia on January 24. The post-mortem

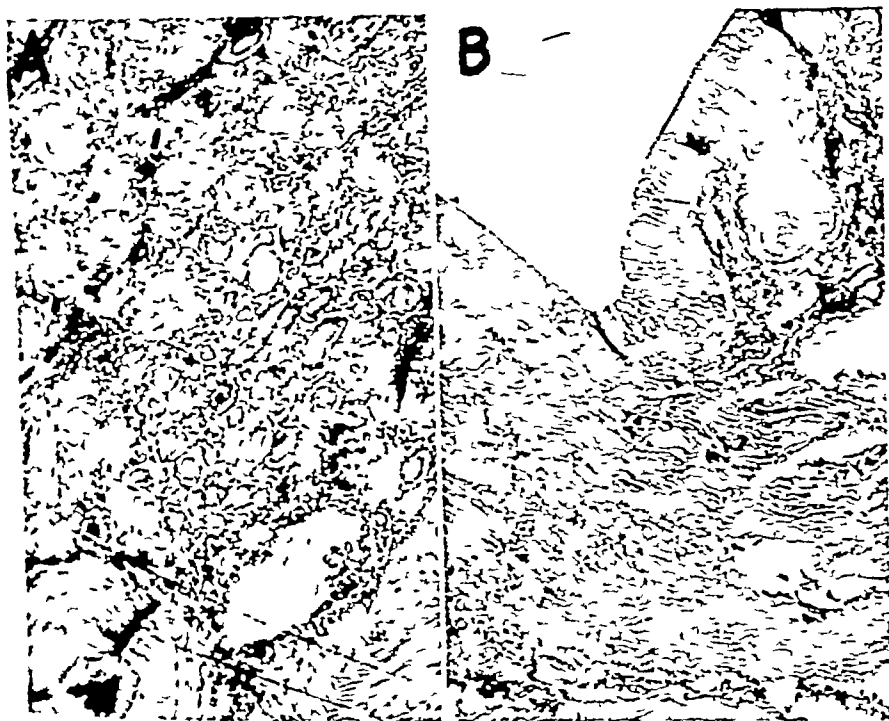


Fig. 20. O. C. A, right kidney. Marked arteriosclerosis. Interstitial fibrosis. Atrophic pyelitis. B, ureterocolic anastomosis 12 years before with intact ureteral and bowel mucosa. Bowel epithelium showed no change.

examination showed a marked hypertensive cardiovascular disease with severe pyelonephritis (fig. 20 A). There was free drainage from each ureter (fig. 21). The sections of the ostra showed mucosal buds (fig. 20 B).

The patient had 10 years of satisfactory renal function following ureterocolic anastomosis. Two years before death irreversible changes began to develop, accelerated by vascular disease and renal damage resulting from chronic infection. Adequate renal drainage remained permanent following the anastomoses. The pericardial orifices in the colon showed no evidence of scarring after 12 years. In reviewing the problem of uretero-intestinal anastomosis it seems that we have not repeatedly during recent years to develop a satisfactory technique which could be followed by permanent adequate renal drainage. The spatula method of Nesbit seems to be ideal for this operation. This operation however, certainly raises the question whether or not a tunnel or sphincter is

seems sure, the prognosis is usually not good. Biopsy must, of course, be done in order to make a definite diagnosis. As with malignancy elsewhere in the body, poor results occur when the diagnosis is made late.

Urethral carcinoma has been treated in many ways. Crutery, local excision, radical excision, radium therapy, roentgen therapy or combinations of these methods have all been used.

It would appear that the treatment should involve two major points, the local lesion and the lymphatic spread, if present. Our choice for treatment of the local lesion is radiation and for the lymphatic involvement would be surgical excision of the involved nodes.

Since 1931 there have been 10,851 cases of all types studied at the American Oncologic Hospital. This institution is devoted to the diagnosis and treatment of malignant disease. Of these 10,851 cases, there were only 3 patients in whom the diagnosis of primary carcinoma of the female urethra could be confirmed by histologic study.

CASE REPORTS

Case 1 (Hospital No. C-3609) Mrs. P., a white married woman, aged 39, was first seen on December 14, 1938. In April 1938, she had first noticed a grape-sized growth at the urethral meatus. She came to realize the presence of this growth after first noticing a slight bloody discharge on toilet tissues. She had no pain or dysuria at this time. The lump increased to the size of a walnut so she went to a physician who "tied it off." One week later the physician excised it surgically. The patient had slight bleeding following this but the area finally healed. Two months later, in July, the lump had returned so she again saw her physician, who removed it with electrosurgery. Ten days after this, she began to have frequency, urgency and terminal dysuria. This continued and in October she again noticed a lump. In December the growth was again removed. Since then she had had less frequency but otherwise her symptoms remained about the same. She was dissatisfied and therefore came to the Oncologic Hospital for advice. Her past history was noncontributory. Her laboratory studies were within normal limits except for urinalysis which showed 1 plus albumin and 5-7 red blood cells and 30-40 red blood cells per high power field.

The external urinary meatus had been enlarged posteriorly (apparently due to previous surgery) so that its diameter was about four times normal. The floor of the urethra was exposed and there was a proliferative, irregular, rounded growth about 2.0 cm. in diameter. It was firm, spongy and protruded somewhat beyond the orifice. The biopsy was reported to show epidermoid carcinoma of the urethra squamous cell type (fig. 1).

On December 15, 1938 a 50 mg. capsule of radium (2.5 cm. in length) filtered with 0.5 mm. of platinum and 1 mm. of brass was placed in the urethra and allowed to remain for 1 hour.

From December 28, 1938, to January 18, 1939, she received deep x-ray therapy (200 k. v.p.—25 m. a 50 t. s. d.—1 Cu 1 Al) through a 1 inch cone, 200 r. a treatment to a total dose of 3000 r. She also received 1500 r. to each of two inguinal areas.

tion are assured. These infections can be minimized or controlled in part with our present effective and antibiotic therapy.

Transplantation of the ureters higher in the gastro-intestinal tract simply intensifies the resorption but tends to reduce infection. We have recently isolated about 12 inches of terminal ileum, anastomosed one end to the colon and transplanted the ureters into the proximal end. This operation was done to reduce infection, but the resorption rate was so great that all of our dogs died of acute uremia. Ormond in 1933 transplanted the right ureter into the sigmoid in 5 monkeys and ligated the left. All 5 monkeys died of resorption uremia. We recently reviewed a patient who had the right ureter transplanted into the cecum (fig. 22) and the left into the sigmoid 1 year previously. She had metabolic disturbances which could not be reversed by the most excellent medical management. She had a miserable existence for nearly two years after uretero-intestinal anastomosis before extreme emaciation caused her death.

Bringing the ureters to the exterior (ureterocutaneous anastomoses) reduces the chances of metabolic disturbance but augments the inconvenience of urinary collection and disposal.

Uretero-intestinal anastomoses are now being performed more frequently with better life results. The simpler techniques are preferable. The use of gadgets and ureteral catheters have become less urgent. It is rather paradoxical that after searching for nearly a century for an ideal technique for uretero-intestinal anastomosis we are now becoming more concerned about some of the side reactions which may follow this unphysiological arrangement and operation. After so many of our discouraging results it is hoped that continued effort will be expended to divert the urine in some satisfactory manner other than the now accepted ureterocolic attachment.

The trend to remove the entire urinary bladder is gaining ground. The late results following cystectomy for papillary carcinoma are decidedly better than the bladder removed for infiltrating carcinoma. Many infiltrating carcinomas have already metastasized at the time of the cystectomy. Radical cystectomies may result in a few additional cures. The surgeon is faced with a serious dilemma. The chance of transurethral cure for papillary carcinoma must be weighed against the unphysiological operation with its chain of untoward complications following cystectomy. With infiltrating carcinoma of the bladder we have little assurance that cystectomy will eradicate the disease. Other possibilities that are now being thoroughly investigated may eventually supplant total cystectomies.

CONCLUSIONS

1. The papuli operation is an easy simple way to attach the ureter to the colon.
2. Use of a tunnel should be preferred wherever possible to minimize infection and damage.
3. Anastomosis (ureter and bowel) attachment usually results in a permanent draining fistula.
4. Uretero-intestinal operations cause serious metabolic disturbance which may be incompatible with life.

of an indwelling catheter for eight days. At present she is alive and free of disease 11 years, 5 months after her first visit to the hospital.

Case 2 (Hospital No. C-8951) B. F., a white widow aged 57, was first seen in January 1948. She gave a history of a vaginal discharge of 1 year's duration. About 7 years prior to this she had heart failure, probably due to arteriosclerotic heart disease. In May 1947, she had sudden numbness in the right side of her body. She was hospitalized and studied and a clinical diagnosis of bronchiogenic carcinoma was made. No pelvic examination was made at this time. In September 1947, she went to another hospital where she was completely examined and a

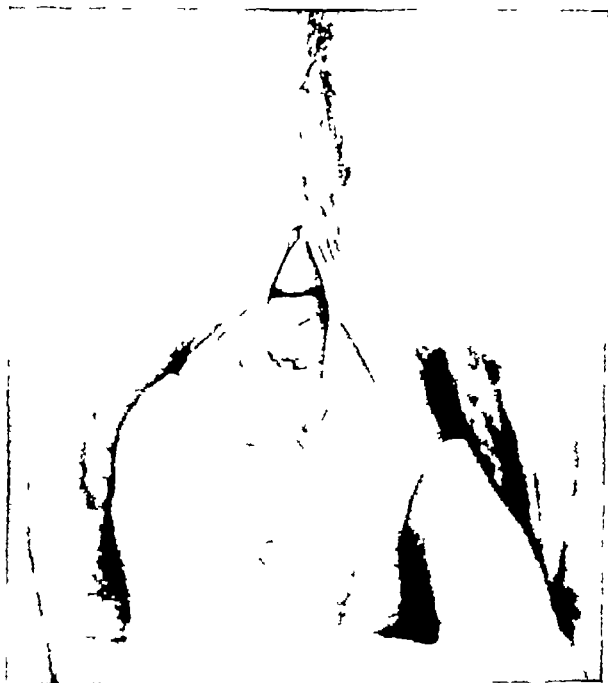


FIG. 2 Case 1—appearance of urethral area April 1950—post radiation

diagnosis was made of primary carcinoma of the urethra with pulmonary metastases. She left this hospital and had a thoracentesis about once every 3 weeks until she was admitted to the Oncologic Hospital.

A friable, fungating tumor, 3.0 cm. in diameter, was seen about the periphery of the external urinary meatus. The tumor extended laterally to both labia minora but there was no fixation to the pubic bone. The orifice was adequate and the infiltration beneath the urethra was minimal. No unusual inguinal lymphadenopathy was present.

The patient had an enlarged heart. The blood pressure was 204/138. A massive left pleural effusion was confirmed by x-ray, which also revealed a rounded area of increased density in the left upper lobe that was thought to be due to tumor formation (fig. 3). A biopsy was reported to show anaplastic carcinoma of the urethra, transitional cell type (fig. 4).

The patient was studied extensively. Multiple thoracenteses were done and

FIBROMA OF THE BLADDER

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Fibroma of the bladder is an unusual tumor. It is a mesothelial growth which may be a pure myoma, fibroma or fibromyoma occurring in any location, but is generally found on the trigone or posterior wall. It is pedunculated, covered with vesicular mucous membrane, and is either submucous, interstitial or peripheral.

Koll¹ in 1923 collected 38 cases and reported one of his own. White² in 1931 reported a case of fibromyoma in a child, 7 years old, and could only find 6 similar cases described in the literature in patients under 20 years of age. Kretschmer,³ who in 1931 made an extensive review of the literature and reported a case of fibromyoma of the bladder, believed that "the prognosis is good, due to the benign nature of these growths, provided there is no large degree of associated pathological change." Other cases have been reported by Smith,⁴ Mangot,⁵ Wershub,⁶ Gersinger,⁷ Martin,⁸ and Pierson.⁹ It is estimated that not more than 50 cases have been reported.

The pathogenesis is vague. Blum¹⁰ suggested that they originated from the hypertrophied bladder muscle secondary to inflammation, while Hager¹¹ thought that they developed from a hydral of Morgagni or lower liver of the utricle. Verhoegen¹² advanced the theory that they developed from a partially atrophied Mullerian body.

Koll described two types of fibroma, a hard and soft, and stated that the former undergoes calcification, fatty degeneration and necrosis as a result of its poor blood supply while in the latter type calcification is rare, but necrosis does occur. He states the size may vary from a hazel nut to one weighing over 3200 gm.

The symptoms vary with the location and size of the tumor. One located near the internal urethral orifice or either ureteral orifice will produce symptoms earlier than one situated some distance from these openings. When the tumor becomes large, frequency, diminished bladder capacity and nocturia may occur. Urgency and dysuria accompany infection.

Hematuria, noted by Kretschmer is the most frequent symptom. Malignant degeneration has been recorded.

The following case was that of a man 71 years old. He was referred by Dr. N. M. Freund in June 1948 with a history of hematuria 4 weeks previously, and which had appeared spontaneously. Other symptoms noted for several weeks

monary metastasis. No autopsy was obtained and no information was available in regard to the condition of the urethra.

Case 2 represents an unusual variety of urethral carcinoma with apparent pulmonary metastases. Because of the patient's generally poor condition and the necessity of radiation therapy elsewhere in the body, the urethral area assumed secondary importance. However, despite a short period of observation, the urethral growth had responded nicely to local radium treatment.

Case 3 (Hospital No. C-9142) F. V., a married Negress aged 50, was first seen on April 14, 1948. She had had an uneventful cessation of her menstrual periods about 5 years ago. About 2 weeks before she was seen at the Oncologic Hospital she noticed some urinary frequency and bloody vaginal discharge. The rest of her history was noncontributory. The pelvic and urethral examinations



FIG. 5 Biopsy, urethra—case 3—epidermoid carcinoma, squamous cell type—100X

revealed nothing of note. The uterus was normal in size and the cervix was intact and did not bleed on manipulation. She was admitted to the hospital and on May 3, 1948, she was examined under anesthesia. Dilation of the cervix and fractional curettage of the cervix and endometrium were performed and no material was obtained. It was noted that "stripping" of the urethra produced bleeding although catheterized urinalysis was negative throughout. For this reason the urethra was slowly dilated and examination revealed a 1.0–1.5 cm area of pocketing on the left posterolateral portion of the urethra just within the urinary meatus. This area was thoroughly curetted and a moderate amount of friable material was obtained. Panendoscopy revealed no extension upward to the bladder. A biopsy was reported to show epidermoid carcinoma of the urethra, squamous cell type (fig. 5).

The patient received an intra-urethral radium application on May 10, 1948 of 250 mg./hrs. and on June 1, 1948 of 300 mg./hrs. The factors were a 50 mg. capsule with a length of 2.5 cm., width of 0.8 cm., and filtration of 0.5 mm. platinum, 1 mm. brass and 1.0 mm. rubber.

The patient has been examined at intervals and when last seen in April 1950 there was no evidence of residual disease.

It was impossible to determine where the tumor was attached to the wall of the bladder as the pedicle could not be observed. Excretory urography was negative except for a slight hydronephrosis on the right side. A large filling defect in the bladder was present in the cystogram.

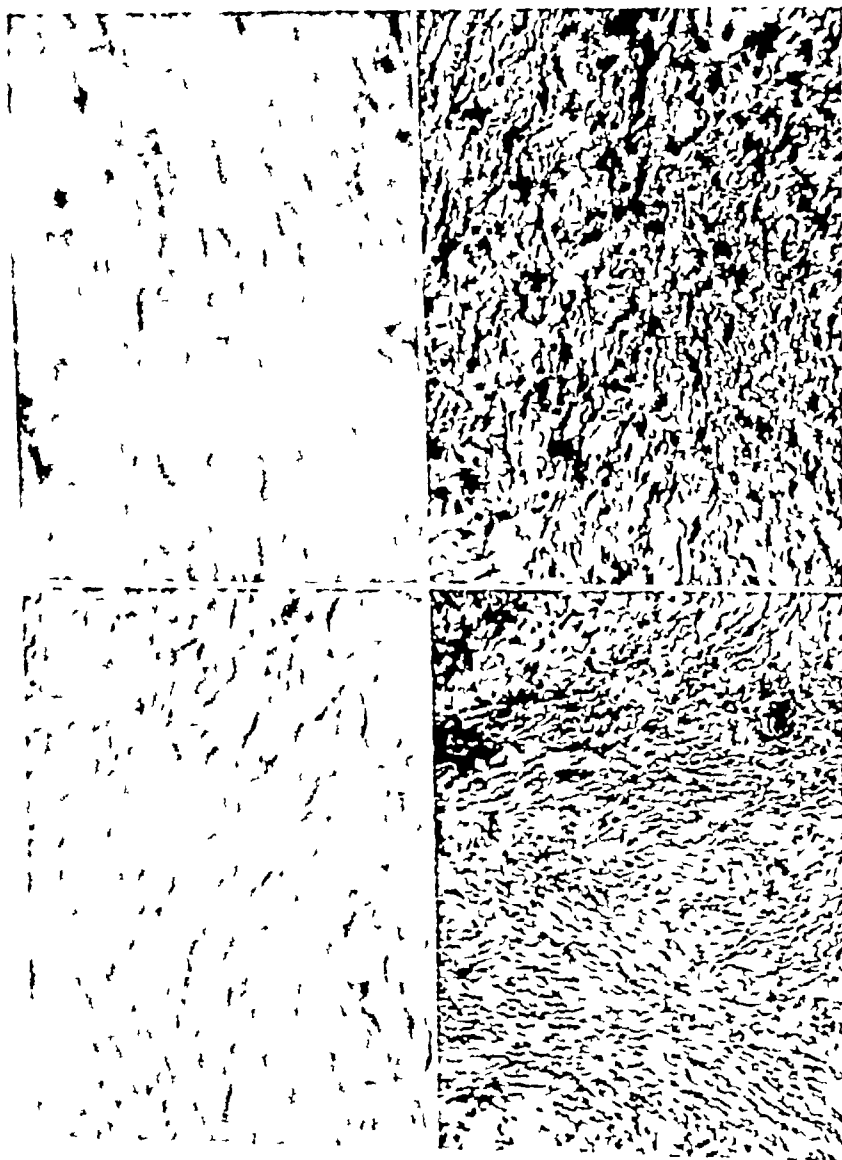


FIGURE 2

CARCINOMA OF THE PENIS

HARRISON C HARLIN

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According to Paget and Billroth, cancer of the penis constitutes 1 to 3 per cent of all carcinomas in the male. Pack and Le Fevre found that the first hundred cases reported by Dean¹ comprised 1.25 per cent of all malignant tumors in males admitted to Memorial Hospital.

ETIOLOGY

Although, as in other forms of malignancy, the etiology is obscure, one factor stands glaringly above all others, chronic irritation. This occurs when the prepuce is difficult or impossible to retract and accompanies balanitis and balanoposthitis. Hard, retained, inspissated smegma is also a definite source of irritation and sets up ideal conditions for the development of penile cancer. Lewis² points out that a retractable prepuce is not insurance against the retention of smegma. Nineteen of his 70 reported cases of penile cancer had retractable foreskins without phimosis and five acquired phimosis during the growth of the tumor.

If the presence of a prepuce with or without associated phimosis acts as such an important causative agent of cancer, what change in the status of potential carcinoma occurs when circumcision enters the picture? Cancer of the penis does occur when circumcision is performed *after* infancy. Although circumcision in the early years of life does give relative protection, circumcision in the later years has little prophylactic value. Dean¹ found that 45 of 120 patients with cancer of the penis required operation to free the glans and that cancer was found when the glans was exposed. In 12 of the 120 cases circumcision was performed several years before the cancer appeared. Lenowitz and Graham³ reporting on 139 cases state that the average median time of development of the malignant lesion was 22 years after the date of circumcision. It is interesting to speculate why cancer develops in these patients after a period long enough to allow regression of any irritation that might have been present at the time of circumcision. Could it be, as has been suggested, that when circumcision is performed in later years the glans may have lost its ability to form a resistant covering and thereby render itself sensitive to the contacts of everyday life? Or is it that the foundation of cancer has been laid in years of irritation provoked by conditions within the preputial cavity and the fundamental trauma of the tissues has already been effected by the time circumcision is performed? The operative procedure (circumcision) itself may in many instances act as a 'trigger' stimulus to an already preexisting lesion.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

¹ Dean A. L. Epithelioma of penis. *J. Urol.*, **33**, 252, 1935.

² Lewis L. G. Radical operation for cure of cancer of penis. *J. Urol.*, **26**, 205, 1931.

³ Lenowitz, H. and Graham A. Carcinoma of penis. *J. Urol.*, **56**, 458, 1946.

The papillary tumors begin as a wart or a nodule springing from the glans or from the mucous surface of the prepuce. These warts increase in number and coalesce. The rate of growth of these nodules varies from individual to individual and as a rule infection supervenes. This infection is aided by interference with the blood supply particularly in individuals with a tight prepuce. Necrosis and ulceration quickly follow so that a foul and sometimes bloody discharge is found draining beneath the prepuce. The prepuce itself may become perforated or completely destroyed by this process.

The flat tumors generally start as small ulcers which appear early in their growth as excavations. These excavations infiltrate deeply and spread laterally involving the deeper tissues of the penis without producing any great changes in the surface tissues. Buck's fascia markedly delays the invasion of the corpus cavernosum and generally prevents that of the corpus spongiosum. These tumors probably originate in the regions of greatest irritation, namely the glans, prepuce, frenum and coronal sulcus.

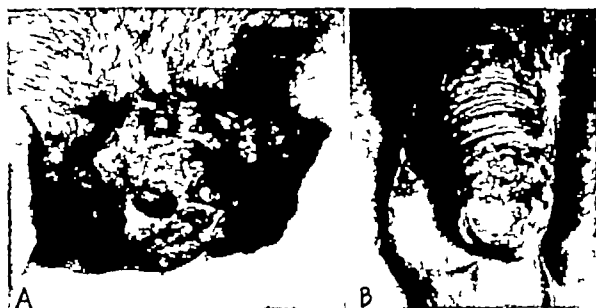


FIG 1 A, squamous cell carcinoma of penis, fungating (papillary) type B, squamous cell carcinoma of penis (flat (infiltrating) type)

The "natural" growth of a penile carcinoma is rather difficult to estimate. Stein recognized the leukoplakic lesions usually observed in these cases as a pre-cancerous stage in the development of these tumors. Mühlpfordt⁶ agrees with this interpretation and believes that many years may elapse before these lesions become clinically and histologically recognizable as malignant tumors. On the other hand, Savatard⁷ described what he termed "psoriasiform carcinoma of the penis" which he believes to be a true carcinoma.

METASTASIS

The penis presents three principal, intercommunicating lymphatic systems:

- 1) The prepuce, frenum, skin and subcutaneous tissues of the penis drain into the superficial inguinal nodes, some of which in turn communicate with the deep inguinal nodes.
- 2) The glans penis and corpus cavernosum drain into a plexus of anastomosing lymph vessels in front of the symphysis pubis. From this plexus lymphatic channels drain into the deep inguinal nodes and external iliac nodes (either by way of the crural canal or the inguinal canal).

⁶ Mühlpfordt, H. *Derm. Woch.*, 87, 1403, 1928.

⁷ Savatard, L. *Psoriasiform carcinoma of penis*. *Brit. J. Dermat. & Syph.*, 52, 57, 1940.

by all successive bowel movements cause further movement through the coats by ulceration or in the case of sharp objects by direct penetration. An inflammatory mass then forms and the foreign body is surrounded. As it continues to be extruded the inflammatory reaction spreads and attachment to neighboring structures such as the bladder may occur. The foreign body then enters the bladder and the tract seals behind it or the tract remains patent.¹¹

During the process of development the course is characterized by predominantly bowel symptoms at first then there is a free interval with no symptoms when the foreign body has penetrated one organ and lies in a loose capsule of granulation tissue. Then as progress continues symptoms develop in the organ about to be entered. Thus a foreign body passing from the bowel is manifested by crampy abdominal pain, loose movements, etc., and then there is a quiet period with no symptoms and then as it penetrates the bladder dysuria, pyuria, hematuria, pneumaturia and fecaluria develop. The time interval varies from a few weeks to years.¹¹

The symptoms and signs of foreign body intestino-vesical fistulas do not differ very much from those of fistulas due to other causes. The most significant findings are 1) pneumaturia 2) fecaluria and 3) passage of urine from the rectum.

Although pneumaturia is very common it is not pathognomonic¹² as it may occur in yeast infections, cystitis emphysematosa and after catheterization and instrumentation. However it is a very valuable presumptive sign. Fecaluria is pathognomonic but is not always present and may occur intermittently depending on the consistency of the stools. Passage of urine in the feces is very important and is related with vesical neck obstruction or severe cystitis with thick walled bladder with marked intravesical pressure.¹

Frequency, urgency, pain and strangury are more marked in foreign body fistula. The intestinal symptoms may also be more severe.

Patients with persistent cystitis and upper tract infection with changing flora and peculiar urinary coloring must be checked for the possibilities of fistula.

The diagnosis depends to a great extent on a precise history of pneumaturia, fecaluria and bowel disturbances. The precise diagnosis may only be arrived

4) In the majority of individuals the lymph nodes are surrounded by fat which by acting as a screen prevents an adequate response by the lymph nodes to radiation

Radium is used when the penile lesion measures 2 cm or less, and has not involved the corpora. Because the majority of penile cancers are radioresistant heavy doses are required for their removal. This intensive treatment stimulates the formation of fibrous tissue which in turn is able to cause contractures. For these reasons extensive lesions are not, as a rule, treated with radium.

Lederman⁹ of the Royal Cancer Hospital in London, although he admits that surgical removal of the primary tumor gives a good prospect for local cure, ventures to offer a radiotherapeutic procedure as an alternative to the admittedly successful surgical method.

Pfahler and Widman advocate electrocoagulation and electrodisssection of the primary lesion. These procedures offer no advantage over surgical removal be



FIG 2 Postoperative simple amputation of penis. Patient capable of performing coitus cause they frequently produce painful and deforming scars—and recurrences of the initial growth do happen.

Although surgical removal is generally used, great diversity of opinion about the proper treatment for the lymph nodes exists. The majority of the advocates of surgery agree that a simple amputation approximately 1.5 to 2.5 cm proximal to any visible or palpable evidence of disease is a satisfactory and safe procedure for handling the site of the primary tumor (fig 2). This particular operation stems from the finding that the tumor metastasizes by embolism. Local recurrences following this procedure are indeed rare.

Frequently, enough of the organ is left to allow coitus. In obese patients and in those whose penile stumps have to be very short, the better procedure is to bring the urethra out of the perineum (fig 3) and avoid the subsequent soiling of the skin by urine. Wherever the urethra is placed, attention must be given to the external meatus. Otherwise strictures may form and give the patient a new complaint. In the occasional patient, interval dilatations of the urethra have to be carried out for years.

⁹ Lederman, M. Radium treatment of cancer of the penis. *Brit J Radiology*, **13**, 393, 1940.

U analysis revealed numerous white cells. The hemogram was normal. Blood sugar 80 mg. per cent, nonprotein nitrogen 33, total protein 6.2, albumin 3.8, globulin 2.4. The acid phosphatase was 2.3.

An x-ray of the abdomen revealed two curved metallic foreign bodies in the approximate region of the sigmoid colon (fig. 1). Excretory urograms revealed normal functioning upper tract. Smear of the urinary sediment revealed gram positive cocci in chains. On culture there were nonhemolytic streptococci. Chest films revealed old healed pleurisy and apical tuberculosis.

Cystoscopy on the day following admission revealed a small fistulous tract in the left dome of the bladder. There was a small opening with mucoid material exuding. Attempts to pass a catheter through the opening were unsuccessful.

Proctoscopy revealed an obstruction at 14 cm. No fistulous tract was seen, but it is believed that obstruction might be associated with inflammatory reaction from the fistula. Unfortunately, the use of colored dyes such as methylene



FIG. 1

1) After simple amputation 1 5 to 2 5 cm proximal to the primary lesion, recurrence is rare

2) In about 50 per cent of the cases of inguinal adenopathy, infection is the cause of the glandular enlargement

3) It has been generally reported that approximately a 20 per cent mortality rate characterizes the radical operation. However, Hudson, Cason and Scott¹ cite 70 cases subjected to radical surgery with an operative mortality of 7 1 per cent

4) One of the principal causes of mortality after groin dissection is infection. This infection is at its height at the time the primary tumor is being treated and regresses after its removal. Therefore, operation upon the groin should be delayed until the infection has subsided. The lymph nodes which were enlarged by infection decrease in size, whereas, those which are enlarged by infiltration of metastatic tissue increase slowly in size. If these nodes do not regress, a biopsy is indicated. If the biopsy is positive for cancer, a block dissection is in order.

Approximately 80 per cent of the extensive primary tumors without metastases respond favorably to this treatment of simple amputation.

TABLE 1 Age distribution of 21 patients

AGE GROUP	NUMBER OF CASES
11-20	1
21-30	1
31-40	3
41-50	5
51-60	8
61-70	2
71-80	0
81-90	1

It is a pity that the general public is so hesitant about seeking competent medical treatment at an early date after the onset of the symptoms of this disease, for early treatment promises more than a 70 per cent "cure," whereas, treatment delayed until metastases have developed gives only a 5 to 15 per cent chance of "cure."

REPORT OF CASES

Twenty-one cases of carcinoma of the penis have been observed at V A Hosp 48, Atlanta, Ga., and Lawson V A Hospital, Chamblee, Ga. during the course of 10 years.

At the time of first admissions to these hospitals, the ages of the patients varied from 18 to 82, the greatest number was found in the 41 to 60 age group (table 1).

As a group these patients had been subjected to several different types of procedures before coming to these hospitals. Nine had biopsy of the primary

¹ Hudson, P B, Cason, J F and Scott, W W. The value of radical operation for carcinoma of penis. South Med J, 41, 761, 1948

surgically showed inflammation and the remaining 50 per cent contained metastases

Table 6 shows the treatment these patients received in V A Hospital 48 and Lawson V A Hospital. Three total penile amputations were done, one because of the extensive involvement of the shaft of the penis, one because the excessive obesity of the patient would have meant soiling the body with urine from the stump. The third amputation included a groin dissection. This patient died after a transfusion with incompatible blood.

TABLE 5 *Inguinal lymph nodes*

Enlarged unilaterally	4
Enlarged bilaterally	8
No enlargement	9
Enlarged glands removed surgically	6
No glands containing tumor	3
No glands only inflammatory	3

TABLE 6 *Surgical treatment in V A Hospital 48 and Lawson V A Hospital*

Total amputation	3
Partial amputation	7
Amputation and bilateral groin dissection (at same time)	2
Simple amputation	1
Complete amputation	1
Biopsy of primary lesion and nodes	8
Bilateral groin dissection	3
Dorsal slit and circumcision	1

TABLE 7 *Results of therapy*

Dead of carcinoma of the penis or metastases	2
Dead of other causes	2
Living without recurrence or metastases	16
Living with recurrence or metastases	1

Only 1 patient thought that trauma might have played a part in the development of his disease, although the trauma occurred 30 years before the development of a lesion.

Nine out of these 21 patients gave a history of venereal disease. Two had had gonorrhea, 3, syphilis, and 4, both syphilis and gonorrhea. The incidence of venereal disease in carcinoma of the penis is definitely higher than that in the general population.

Four (19 per cent) patients were dead at the time of this report. One died of uremia due to hypertensive cardiorenal disease 8 years after simple amputation and bilateral groin dissection. There was no evidence of tumor whatsoever at the time of death. Three days after total amputation the second died in uremia, which followed a transfusion with incompatible whole blood. The third death was due to generalized metastases 4 years after radical amputation and bilateral

In July and August 1939 because of infiltration beneath the urethra, she received 5 local radium treatments as described above for 1½ hours each at weekly intervals for a total dose of 375 mg. hours. Following this she received deep x-ray therapy between August 16, 1939 and September 15, 1939 to a total dose of 3000 r. The factors at this time were the same as previously except that the filtration was ½ mm. Cu. and 1 mm. Al.

She was seen at intervals in our clinic until 1942 and her condition was thought to be satisfactory. In May 1942 she was seen at another hospital because of urinary retention and a suprapubic cystotomy was performed. She was then referred to the Oncologic Hospital. After admission it was possible to identify the external urinary meatus which was probed and catheterized successfully. The cystotomy tube was removed and the patient voided again without difficulty. The cystotomy opening closed spontaneously. She was seen at intervals in the



first diagnosed One ($33\frac{1}{3}$ per cent) of these 3 is alive at the time of this report, 3 years following simple amputation with bilateral groin dissection, with no evidence of the disease Two ($66\frac{2}{3}$ per cent) of these 3 are dead Each died of generalized metastases, one 2 years after therapy, the other, 4 years Each of these two had radical penile amputation, bilateral groin dissection and postoperative radiation

Group 2 Patients without evident metastases when primary disease was first diagnosed Eighteen (85.7 per cent) of the 21 cases had no evidence of metastases when the primary was first diagnosed Sixteen (89 per cent) of these 18 cases were alive at the time of this report With one exception each of the 16 shows no evidence of the disease This individual refused treatment Two (11 per cent) of these 18 cases are dead One died of hypertensive cardiorenal disease 8 years following simple amputation There was no evidence of cancer at death The other patient died 3 days after total amputation in uremia secondary to receipt of incompatible blood Three (18.7 per cent) of the 16 living cases had local excision or fulguration with postoperative radiation Three (18.7 per cent) of the 16 living cases had complete amputations Ten (62.6 per cent) of the 16 living cases had simple amputations, 1 of these had a bilateral groin dissection and 2 of them, postoperative x-ray therapy

SUMMARY

Penile cancer constitutes 1 to 3 per cent of all carcinomas in the male

Although the etiology is obscure, chronic irritation stands glaringly above all other factors Hard, retained, inspissated smegma is a definite cause of irritation and sets up an ideal condition for the development of penile cancer

Jews, who undergo ritualistic circumcision in early infancy, do not suffer from carcinoma of the penis The Mohammedans who practice ritualistic circumcision later in life (between third and tenth years) are afforded relative protection from penile cancer Penile cancer, then, occurs almost exclusively in the uncircumcised, particularly in those with phimosis, and occasionally in those circumcised in adult life Circumcision done in infancy gives complete protection and is therefore the number one prophylactic measure

Two types of carcinoma of the penis are described, the papillary and the infiltrating (flat)

Several varieties of treatment have been used for the management of this malignancy, these treatments include surgery, electrosurgery, deep x-ray and radium therapy and their combinations We are in favor of the conservative surgical approach, the principles of which are as follows

1) Simple amputation approximately 1.5 cm. to 2.5 cm. proximal to any visible or palpable evidence of disease

2) Use of a perineal urethral opening only in instances where soilage by urine would otherwise occur (short residual stump, in the obese)

3) Groin dissection, in cases with adenopathy due to metastases, after the primary tumor has been treated This time interval (2 to 3 months) allows the

histological examination of the thoracentesis performed. However, our pathologist was unable to make a cytologic diagnosis of carcinoma on the cells in the removed fluid. X-ray studies revealed narrowing of the bodies of the eighth and tenth dorsal vertebrae with irregularity of the superior surfaces which was thought to be due to metastatic disease. From February to September the patient received three courses of x-ray therapy directed to the left chest and one course of x-ray therapy directed to the left supraclavicular area. Because of several episodes of heart failure associated with auricular fibrillation specific therapy to

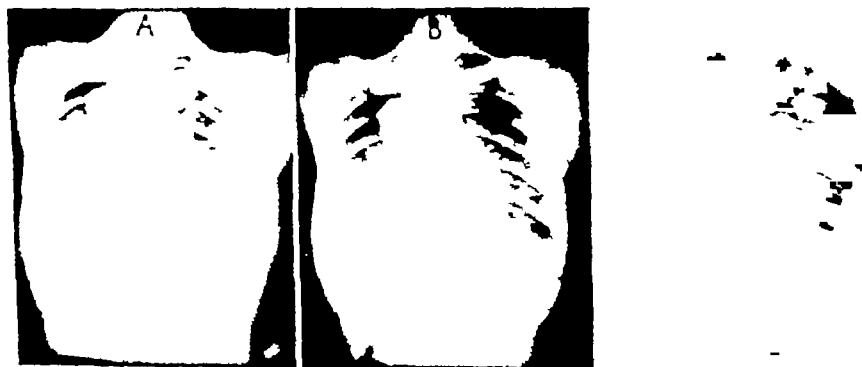
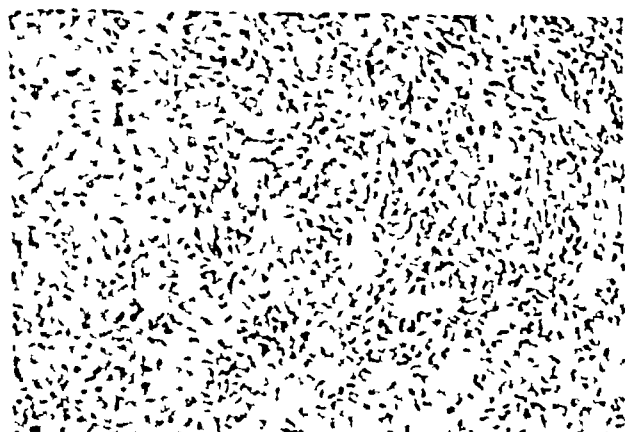


Fig. 3 A—X-ray chest—case 2—January 3, 1948.
 Fig. 3 B—X-ray chest—case 2—February 11, 1948.
 Fig. 3 C—X-ray chest—case 2—November 11, 1948.



RETROPERITONEAL LYMPH NODE RESECTION THE INTERCOSTO-INGUINAL APPROACH

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Hinman et al, Lewis, and others have described the technique of retroperitoneal lymph node resection. Sargent at the 1951 meeting of the American Urological Association presented a movie of his technique, and Vallett presented a movie adapting the Nagamatsu approach. The transthoracic approach has been adequately described by Chute.

The large number of cases of testicular tumor seen at this hospital has given ample opportunity for development and improvement of a more efficient approach to the retroperitoneal area.

The incision advocated by Hinman extended from the inguinal ring to the tip of the twelfth rib and then paralleled that rib posteriorly. Lewis made his incision to the tip of the eleventh rib. Sargent presented the figure 7 incision with the horizontal arm from the tip of the twelfth rib to the edge of the rectus muscle.

These approaches have been used at this hospital in many cases. It was recognized that the most difficult part of the operation consisted of the removal of the metastatic nodes at the level of the renal pedicle on the left and between the pedicle and the entrance of the internal spermatic vessels on the right. In an effort to gain more adequate exposure of this area as well as the pelvic portion using one incision, the approach here presented was developed.

The patient is placed on the operating table in supine position with a strap across his knees. The shoulder of the operative side is elevated with a sandbag and a smaller sandbag is placed under the loin. This keeps the hips level, hyperextends the midabdomen and elevates the rib cage of the operative side. The patient is braced on the table to allow lateral rotation of 10 to 15 degrees if necessary.

If the testicle has not been removed previously, as in the case of many of the patients at this hospital, it is removed through an inguinal incision. It should be stressed that the inguinal approach should always be used when testicular tumor is suspected. This allows clamping of the cord prior to manipulation and prevents secondary infection of the radical incision due to previous trans-scrotal orchiectomy.

The 4-cm incision for the gland resection is made from the external inguinal ring to the tip of the eleventh rib, and then carried between the tenth and eleventh ribs to the posterior axillary line.

The external oblique muscle and fascia are divided in the line of their fibers. The internal oblique, and transverse abdominal muscles are then transected. The intercostal muscles are divided to the midaxillary line. The pleura is identified and retracted posteriorly. If the pleura is accidentally opened it is immediately sutured under positive pressure anesthesia. In unusual situations, where more

In case 3 the history of bloody vaginal discharge suggests a gynecologic basis for her complaint. In view of the essentially negative gynecologic examination in continuation of the urethra and bladder were carried out and the proper diagnosis made. At present the patient is living and free of disease 2 years after her initial entry to the hospital.

From the aspect of theoretical radiation physics, primary urethral carcinoma should be an ideal lesion to treat by means of local radium therapy. The radium capsule may be placed in the urethral meatus with the growth about the periphery of the capsule. In our cases the capsule was adjusted to the proper position in the urethra and then sutured in place to the labiae so that an accurate application is made for the desired number of hours. It is thought that growths that are localized to the urethra may be adequately managed by means of intra-urethral radium applications. If the growth is more extensive, but still localized, intra-urethral radium and vaginal cone therapy may be utilized. If the growth has metastasized to the inguinal areas radical lymphadenectomy should be done.

The highest percentage of 5 year survivals (44.1 per cent in 35 patients) has been reported by Ericke and McMillan. They use a combination of local radium therapy and local excision.

SUMMARY

A brief survey of the incidence of primary carcinoma of the female urethra is given.

The importance of biopsy of lesions about the urethra, even those which clinically appear benign is stressed.

The management by means of radiation for the local lesion and surgery for distant lymphatic spread is thought to be the treatment of choice.

The history of a patient (case 1) successfully treated by radiation is presented.

The history of a patient (case 2) with apparent pulmonary metastases is presented.

The history of a patient (case 3) with a chief complaint of vaginal bleeding attributable to urethral carcinoma is presented. The importance of examination of the urethra and bladder is emphasized, even in patients with complaints apparently of gynecologic nature.

Submitted September 19, 1954

The wound is closed in layers. Either silk or catgut may be used. If the radical is secondary to a trans-scrotal orchiectomy, probably catgut should be used.



FIG 2 Lateral retraction of ureter, stripping nodes from aorta and vena cava. Note excellent exposure of renal pedicle and large node at this level which was positive for tumor.



FIG 3

and the wound drained. In primary operations, silk without drainage can be used safely.

Figure 3 shows the incision on the right and on the left side.

The operation must be kept as bloodless as possible. If a little bleeding is allowed to continue it soon gets ahead of the surgeon and trouble may develop.

A GRANULOMA OF THE TESTIS OF UNKNOWN ETIOLOGY

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We recently have observed 5 patients with operatively removed unilateral granuloma of the testis. Tuberculosis, syphilis, other infectious agents, or trauma could not be implicated in any of these cases. Finding these cases excited our curiosity and caused us to examine textbooks and literature to see if such a condition had been previously described. Literature sources are vague about the subject, most cases which were in any way similar to ours from the clinical standpoint are described under the terms of "idiopathic epididymo-orchitis," "nonspecific epididymitis," "traumatic epididymo-orchitis," and "epidemic epididymo-orchitis." The cases in the literature were usually bilateral and followed a varied clinical course which healed, either without residue or with atrophy. Unfortunately, from the standpoint of understanding this lesion no orchiectomies were performed. Since descriptions of the gross pathology and photomicrographs are lacking, we are uncertain as to the exact status of the cases described.

It is our belief that the lesion which we describe may be of some considerable clinical importance since these cases may be confused with tumor of the testis and for this reason unnecessary orchiectomies performed.

Our 5 cases were marked by unilateral, slowly progressive enlargement of the testis with moderate or no local fever and little or no general systemic reaction. They occurred in white men aged 58, 64, 69, and 82 years of age. None of the cases had a history of trauma or strain, nor could infectious diseases be connected with the granulomas. Pathologically they showed a somewhat enlarged testis with marked fibrosis and microscopically a heavy infiltration of chronic inflammatory cells with seminiferous tubule destruction and atrophy. From the morphological standpoint they comprise a single entity, although we have little indication of any possible etiology.

CASE REPORTS

The cases which we wish to report are listed in the order in which they were encountered.

Case 1 A 58 year old white man was first seen in his home on December 15, 1946. His chief complaint was pain and tenderness in his right testis. Upon physical examination the only significant finding was moderate swelling of the right testis and redness of the right scrotum. There was tenderness to palpation in the right groin but no lymph nodes were palpable. The patient stated that he had had this condition for a period of 8 to 10 days during which time the testis had steadily enlarged and become more painful. The testis was cold, pinked. It was noted that the epididymis was not greatly enlarged.

After 3 days of symptomatic treatment, no change was noted in the condition of the testis. The patient was admitted to the hospital. Laboratory data white

but discrete and nontender. The prostate was enlarged grade 1, nontender, and firm.

A chest x-ray on November 10, 1949 revealed minimal emphysema and fibrosis in both lung fields.

An excretory urogram showed no unusual findings. Urinalysis revealed occasional white cells, 10-20 red blood cells. Blood count revealed Hemoglobin 14, red blood cells 4.33 million, white blood cells 10.6, with a slight shift to the myeloid series. Thirteen days later the hemoglobin was 11, red blood cells 4.20 million, white blood cells 5.2 normal differential. The serology was negative.

A right orchiectomy with excision of involved scrotal tissue was performed November 16. The scrotal wound healed without drainage and the postoperative course was uneventful. Temperature was normal except the day of operation when it was 100°F.

He returned to the urology clinic April 11, 1950 with a history of excellent course until April 7 when he began noting discomfort and swelling in the right groin which had gradually increased in size. Examination revealed a painful mass 3 cm in diameter in the right inguinal region. It was smooth, tense, and fixed to the deep structures. He was sent home on bed rest, local heat, and fluids and has not returned to the clinic.

Pathological report: "Specimen is a large testis measuring 5 cm in diameter. It has a uniform tan color and soft consistency and has been sectioned. The tubules are fibrosed. The capsule is slightly thickened and proceeding from the lower pole upward is another mass of tissue composed of convoluted yellow components and solid white components. The spermatic cord extends upward about 2.5 cm above the testis. A section is taken from the extreme upper limit of the spermatic cord. The lower pole of the testis has a 3 by 2 cm block of skin attached. Five sections are taken. *Microscopic*: This section is skin and testis. Beneath the normal epidermis the dermis and underlying connective tissue are seen to contain massive amounts of chronic granulation tissue. The tubules of the rete testis are dilated and contain a few acute inflammatory cells. The intervening stroma contains masses of chronic inflammatory cells. The seminiferous tubules are markedly thickened and edematous with the cellular lining being broken away. The stroma contains acute and chronic inflammatory cells and plasma cells (fig. 1). *Diagnosis*: Chronic granuloma of testis, nonspecific."

Case 3: A 69 year old white man was first seen in the urology clinic December 6, 1949 at which time he gave a history of four attacks of left testicular swelling and pain, accompanied by fever and chills, and subsiding in 3-5 days on home remedies and rest, the last time with penicillin. On three occasions he had bloody urine (following the onset of the attacks). The swelling completely subsided on each occasion except the last. The last attack began 6 weeks before admission to the hospital, November 2, 1949, with swelling, pain, chills, and fever. Three days after the onset his local physician gave him penicillin daily with subsidence of pain and temperature, but no regression of swelling.

Examination on December 6, 1949 revealed a 4 by 8 cm, firm, smooth, nontender mass in the left scrotal sac, freely movable and having no increased heat

Colby and Smith advise groin dissections in all except the earliest cases. They performed block dissections on 32 patients with cancer of the penis and of the 32 eleven had no clinically palpable inguinal nodes. In 4 of the 11 cases, however, the tissues removed contained neoplastic deposits.

Of 100 cases of carcinoma of the penis, Barringer¹¹ found 37 cases of groin metastases. Twenty-seven per cent of these 37 were controlled for periods of 1 to 9 years. One had a radical groin dissection, four had exploration of glands and radon seed implants, 4 had external radiation alone, 1 had no treatment. Each of the 27 remaining patients died of carcinoma, although 4 of them lived for 2 to 3 years, and 1 for more than 3 years. One-half of the deaths occurred during the first year. Barringer concluded that since both surgery and radiation proved impotent in dealing with inguinal metastasis from cancer of the penis, combination of external radiation and radon seed implantation by means of



and is uniformly light tan in color. It is very firm to touch and sections with moderately increased resistance. One section of testicle and one section of the vesicular bundle at the superior portion is taken. *Microscopic* Sections of the testis show the tunica vaginalis to be thickened by connective tissue proliferation containing numerous round cells. The normal architecture of the remainder of the testicle is destroyed. The rete have been replaced by scar tissue which forms ghost remnants of usual histological pattern. This connective tissue is loose and there is an epithelioid reaction with numerous round cells and occasional foreign body giant cells. This chronic granuloma has a tubercle like appearance but lacks the necrosis and Langhans type of giant cell to make such a diagnosis. This reaction extends to the epididymis but this is not as extensive

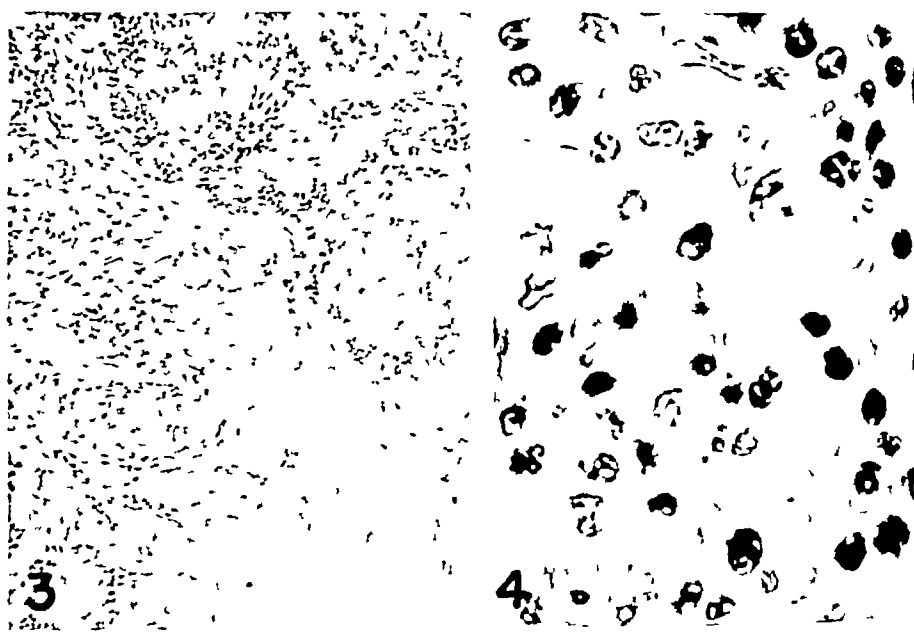


FIG 2 Case 3 3, Low power view showing fibrosis and inflammatory cells 4, High power view of same field showing type of inflammatory cells H + E stain

is seen in the testis proper. The reaction is nonspecific (fig 2). *Diagnosis* Chronic granuloma of the testis and epididymis. *Etiology* undetermined."

Case 4 An 82 year old white man gave a history of gradually increasing painless enlargement of the left testis during the past 3 months. He was admitted to the hospital on December 18, 1949. A complete history and clinical work up gave no indication of the cause of the testicular swelling and a few days after admission an orchiectomy was performed.

Pathological report Specimen is a testis which measures 3 by 3 by 4 cm. The parenchyma is tan in color and soft in consistency, it has a uniform architecture. The epididymis shows some thickening with white fibrous strands. The seminal vesicles are hard. No evidence of tumor is seen. Three sections are taken. *Microscopic* Sections of the testis show the rete to be heavily scarred with this scar

thickening and some edema. Four sections are taken for study. *Microscopic*. The scrotum, epididymis and testis are the site of a chronic granuloma. There is no evidence of malignancy or of tuberculosis. Several sections show a round calcified mass. This calcified mass has a foreign body giant cell around it. *Diagnosis*. Chronic nonspecific granuloma, left testis."

In reviewing this case the finding of a small calcified mass suggested that we might be dealing with an old case of filariasis. The patient, however, gave no history of having lived in any other area, and as far as can be determined there have been no cases of filariasis in this section.

DISCUSSION

We have described 5 cases of morphologically similar orchitis. They were unilateral, occurred in men past the age of 55 years and gave little general symptoms. Locally they were marked by swelling and fibrosis. The only case which we could find in the literature similar to these are listed under the term idiopathic epididymo-orchitis,¹ and various other titles.²⁻⁶ It is difficult to be certain that the cases given in the literature are similar to the ones which we report. Among the idiopathic group¹ it is admitted that there is an acute epididymo-orchitis without antecedent infection either local or general, or evidence of trauma. The cases reported were in young men in their late teens or mid-twenties. Some cases were unilateral. Recognition is made of hematogenous infection of the testis from a primary focus, which occasionally occurs. It is postulated that most epididymo-orchitis is produced by infection reaching these structures by way of the excretory canal or they are thought to be of toxic nature.² These postulates do not seem to fit our cases since, if the postulates are correct the infection or damage should be bilateral.

The subject of nonspecific epididymitis has not been treated extensively in the literature.³ The greatest number of reported cases are in young men and are bilateral. The reported cases are nonsuppurative. The duration is usually limited to 6 to 8 weeks and the inciting factors are unknown. They leave little, if any, residue.

The question of trauma enters into the discussion since many such cases are reported.⁴⁻⁶ This does occur as a distinct clinical entity, though infrequently. Some authors⁵ consider either direct trauma or so-called strain as being the mechanism which precipitates a latent infection, or causes spread of infection by way of the excretory ducts. These cases do undoubtedly occur but whether or not these factors are important in our 5 cases is doubtful. All of our cases showed clear urine, as far as infection is concerned, and none of them gave a history of strain or trauma. The strain-infection idea falls short of adequate

¹ Bowen W. H. *Guss Hosp Rep*, **83** 112-117, 1933.

Clem J. G. *Urol & Cutan Rev*, **34** 159-160, 1930.

² Hughes, E. C. *Proc Royal Soc Med*, **36** 323-326, 1943.

³ Handley, R. S. *Lancet*, **1** 779-781, 1946.

⁴ Iwell G. H. *J A M A*, **113** 1105-1109, 1939.

⁵ Amdur, M. I. *Ind Med*, **12** 371-373, 1943.

from dissection which were followed by deep x-ray therapy. The fourth and final death to date occurred 2 years following therapy similar to that given the third patient. Generalized metastases were discovered at autopsy.

One (5 per cent) patient who has developed iliac node metastases is still alive 1 year and 8 months after refusing treatment. At the time of his initial examination his tumor, an early small grade 1 epidermoid carcinoma showed no evidence of metastases.

Table 8 summarizes the 16 patients (76.2 per cent) living without any evidence of recurrence of the initial lesion or metastases.

Complete amputation in each instance was performed in order to avoid soiling the body with urine. The residual stump in two individuals would have been

TABLE 8. *Patients living without evidence of disease*

INITIAL TUMOR	CASE NO.	TREATMENT	PERIOD SINCE OPERATION
Small ulcer	1	Simple amputation	3 yrs. 6 mos.
Penile ulcer	2	Simple amputation	6 yrs. 4 mos.
Ulcer of urethra	3	Simple amputation	
		Post op. x-ray therapy	7 yrs.
Small ulcer	2	Simple amputation	1 yr. 4 mos.
Penile ulcer	2	Simple amputation	2 yrs. 7 mos.
		Simple amputation	1 yr.
Ulcer of urethra	1	Simple amputation	
Metastases		Belly groin dissection	3 yrs. 6 mos.
Penile ulcer	1	Complete amputation	0 yrs. 6 mos.
Penile ulcer	2	Local fulguration	
		Post radiation	10 yrs. 4 mos.
Small ulcer	1	Simple amputation	11 yrs. 3 mos.
Penile ulcer	2	Simple amputation	
		X-ray therapy	8 yrs. 4 mos.
Penile ulcer		Complete amputation	0 yrs. 2 mos.
		Local fulguration	2 yrs.
		Simple amputation	4 yrs. 2 mos.
		Complete amputation	3 yrs. 2 mos.
	1	Local fulguration	
		Local x-ray	27 yrs.

INTERSTITIAL CELL GROWTH OF THE TESTIS EVIDENCE FOR ORIGIN OF THIS CELL FROM SEMINIFEROUS EPITHELIAL CELLS

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The possible origin of interstitial cell growths from the epithelial cells of the seminiferous tubules of the testis has been both confirmed and denied.¹ From examination of an unusual cell growth of the testis and review of the literature on this subject, we wish to again call attention to this aspect of the subject. In addition to a study of the cell of origin of interstitial cell growth, a second problem is the exact category into which such growths should be classified. Are they hyperplasias or neoplasms? The differentiating criteria are quite indefinite. We wish to present our case since it exhibited certain morphological features which may contribute to better understanding this complex problem.

The number of reported cases of interstitial cell tumor in man total approximately 37 since the first case was described in 1906.

NORMAL STRUCTURE AND OCCURRENCE OF THE INTERSTITIAL CELLS¹

Touching upon the major morphological features, the interstitial cells of the testis, Leydig cells, are either connective tissue or epithelial cells, lying in the testicular stroma between the seminiferous tubules. The cells are large and irregularly polyhedral, transition forms are common. The nuclei are usually pale, spherical and eccentrically placed in the cells and contain a sparse amount of chromatin. One, and occasionally two, nucleoli are found. One feature of the normal cell is various inclusions found in the abundant cytoplasm. In the fresh state the protoplasm is filled with highly refractile granules, a large part of which are fats and lipoids. Numerous brownish granules of various size, having properties of waste pigment, lipofuchsin, are present. Other inclusions are droplets of colloid-like substance of an indefinable nature and peculiarly heavily stained, rod-shaped crystalloids.

The interstitial cells vary considerably in number in different persons and at different ages. In the fetus the cells are numerous, after birth they are reduced in number being replaced by connective tissue and by eight years of age few are found. From the time of puberty the cells increase in number. Pigment appears at adulthood and at this time the cells become distinctive and their identification more certain. They are usually collected in groups of four to five but sometimes as many as fifty will be found. During adult life the cells decrease in number, so that frequently they are hard to find. Usually, however, though reduced in number, they are more numerous than prior to puberty. Finally, with old age

¹ Rasmussen, A. T. Interstitial Cells of the Testis in Cowdry's Special Cytology 2nd ed. New York (3) 1673 1932.

² Maximow and Bloom. Textbook of Histology Philadelphia W. B. Saunders Co 4th ed. p. 524 1942.

³ Avery, I. B. Developmental Anatomy Philadelphia W. B. Saunders Co, p. 286 1942.

infection to subside for infection is at its height at the time the primary tumor is being treated.

Approximately 80 per cent of the primary extensive tumors without metastases respond favorably to this treatment of simple amputation. When metastases are present there is about a 15 per cent chance of 'cure'.

I wish to express my appreciation to Dr. Simon Krantz, Chief of the Tumor Registry for his advice and cooperation in making available the charts and follow-up data on these cases of carcinoma of the penis.

My thanks also to Messrs. Thomas W. Scott and Frank C. Roberts of the Medical Illustration Division for their preparation of the medical photographs.

2, Vesou St., Brooklyn 15, N. Y.

3 cases of hyperplasia showed involvement of adjacent structures. Three cases of hyperplasia, one case of local tumor and all malignant tumors showed mitoses. There were metastases in the malignant cases.

They concluded that large collections of interstitial cells are not necessarily pathologic, that multinucleated cells and cells in the tunica albuginea and epididymis do not necessarily indicate invasive growth, and that the only criterion for malignancy is metastasis. However, if the testicle of a patient contained an increased number of interstitial cells, especially if the tubules were partially or completely destroyed, his case should be followed for at least ten years before a decision is reached concerning the malignant nature of the tumor. One hundred and twenty-five different tumors of the testis were examined by Moon and Hüllinghorst⁷ because of the increase in interstitial cells in all embryonal carcinomas of the testis, and because of the fact that there was no instance in which there was a positive Friedman test and an absence of stimulation of interstitial cells they suggested the presence of hyperplastic interstitial cells as evidence for the presence of carcinoma of the testis.

Nation, Edmonson and Hammock⁶ reviewed the literature to 1944 and presented 3 new cases, making a total of 26 cases that they believed to be interstitial cell tumors. Twenty of these cases were benign, of these, nine showed endocrine changes. Six were malignant, none showed endocrine changes. The endocrine changes occurred in patients from 5 to 42 years of age. Six children were included, they showed precocious bodily and sexual development, and one showed gynecomastia. The three adults showed only gynecomastia. Following removal of the tumors, two of the children's endocrine abnormalities completely regressed, two partially regressed and two showed no change. One adult obtained complete regression, one partial regression and the other no regression. There was no correlation between the time the tumor was present and the amount of regression obtained from treatment. These authors added two distinctive growth characteristics of all interstitial cell tumors, *viz*, tumors are either macroscopically or microscopically nodular and the tumors are yellow to yellow-brown in color. They further submitted the typical tumor cell as being a liver cord-like cell with round to slightly oval nuclei, and eccentric punctate nucleoli.

Since the review of Nation⁶ notable cases have been the malignant case of Neeve and Marsh in 1944,⁸ the benign case of Scully and Parham in 1948,⁹ the debatable case of Wilbur and Burger in 1948¹⁰, and the benign case of James and Shape in 1950.¹¹

CASE REPORT

A 76 year old white man had a left hydrocele of the cord 25 years prior to his first examination. Since that time, he had had fluid withdrawn from this hydrocele approximately four times a year, in later years as much as 200 cc. coffee colored fluid were withdrawn at a time. He was seen at this hospital in 1945, where a large hydrocele on the left was found. Hydrocelectomy was refused at

⁷ Moon, H. D. and Hüllinghorst, R. I. *Am. J. of Path.*, **24**, 1067, 1948.

⁸ Neeve, R. H. and Marsh, F. J. *Path. & Bact.*, **56**, 575, 1944.

⁹ Scully, R. L. and Parham, A. R. *Arch. Path.*, **46**, 229, 1948.

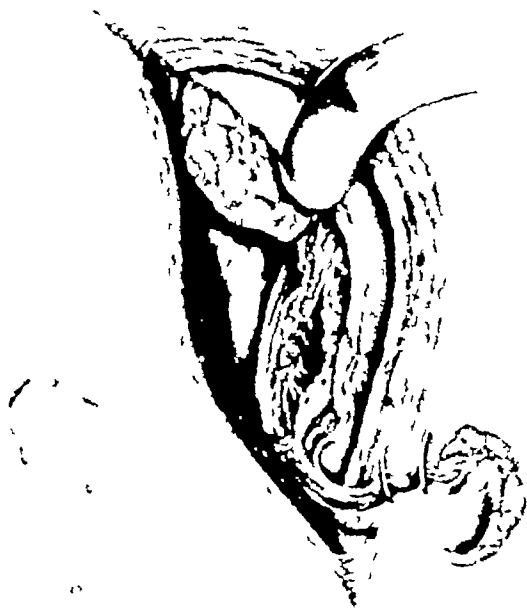
¹⁰ Wilbur, I. F. and Burger, R. A. *J. Clin. Endocrinol.*, **8**, 390, 1948.

¹¹ James, D. C. and Shape, R. D. *J. Urol.*, **63**, 718, 1950.

If exposure might be necessary, the eleventh rib is resected. In 2 cases the tenth rib was resected and a thoracolumbar approach used.

The spermatic vessels are isolated from the peritoneum in their midcourse because that allows easier dissection from the peritoneum at their point of junction. The vas is dissected free, divided and ligated as low as feasible. Complete removal is not necessary, since a metastasis has never been found along its course. The spermatic artery and vein are separated, divided and ligated within 1 to 2 cm. of the great vessels.

The lymph node resection is then begun. This may be started at the renal pedicle or on the external iliac vessels. Both methods have been used and it is felt that there is no appreciable difference. For the purpose of simplicity the resection from caudad upward is described and illustrated.



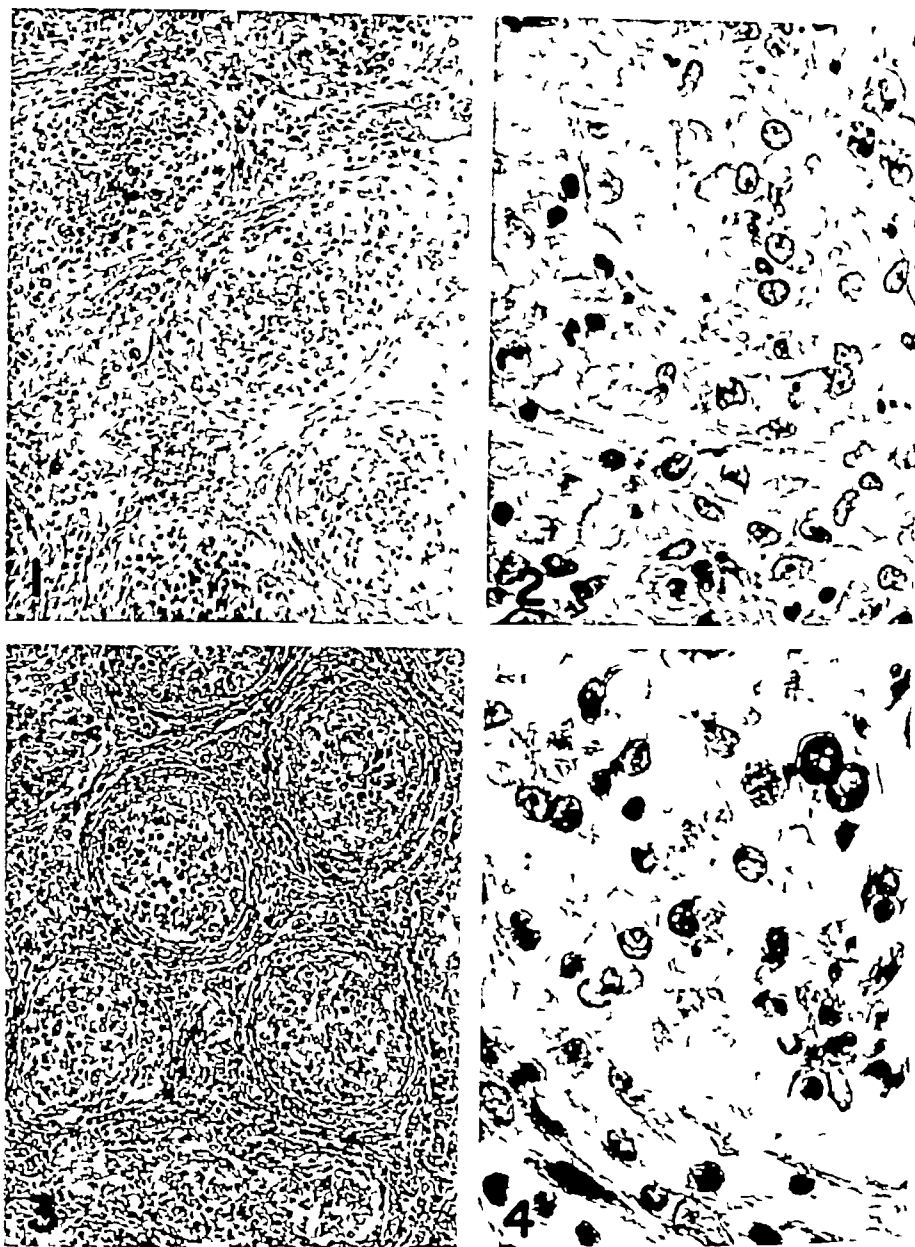


FIG. 1. 1 Low power view. HE stain of interstitial cell tumor. Note how cells tend to form circular arrangements, the kind of arrangement to be expected if cells followed pattern of seminiferous tubules. 2 High power view from central portion of low power field shows typical characteristics of interstitial cells. Namely, large cells with abundant pink cytoplasm with large hyperchromatic nuclei. HE stain. 3 Low power Masson stain of tumor shows connective tissue arrangement. Framework of connective tissue is arranged in circular fashion. 4 Masson stain. High power view of section on left which shows typical cell characteristics of interstitial cell tumor.

interstitial cell tumor Nation et al.⁶ diagnosed the second case of Bonser and Hawksley¹³ to be malignant, presumably because of its invasion of the tunica vaginalis. However, by applying Warren and Olshausen's work⁴ we find the tumor benign. Wilbur and Burger¹⁰ presented their case as an unusual case of hyperplasia. Because of the massive involvement of the testis by interstitial cells, which both replace and displace tubules, we believe that it is a benign interstitial cell tumor. (We have examined their original slides in this case.)

Where do these disagreements lead us? It is obvious that the interstitial cell is not understood as to origin and function. The criteria for origin, and for diagnosis, of hyperplasia and tumor, benign or malignant, are indefinite and weak. Different authors draw conflicting conclusions. Jemerin⁵ concluded that hyperplasia was always focal though widespread and intertubular. Warren and Olshausen⁴ infer that hyperplasia may be intratubular and may even destroy tubules within a given area. Jemerin said the lesion in neoplasia is well demarcated and that there is absence of proliferation and stated that many cases of invasion of the tunica occur and that this is no criteria for malignancy. However, Nation et al.⁶ presumably thought Bonser and Hawksley's¹³ second case malignant due to the invasion of the tunica.

In summation, most authorities agree on the following: 1) Hyperplasia occurs with a decrease in spermatogenesis, normally and pathologically. 2) There is no specific age group for interstitial cell tumors. 3) Grossly the tumors may be yellow to reddish brown and in enlarged testes, whereas hyperplasia occurs in small testes. 4) The microscopic characteristic of the neoplastic cell is that it closely resembles dedifferentiated interstitial cells and Reinecke's crystalloids are always absent from tumor cells. 5) The interstitial cells are the primary source of androgen. 6) Interstitial cell tumors may cause endocrine changes.

We believe the lesion in our case to be, what has previously been classified as a local interstitial cell tumor of the testis. Its characteristics are in agreement with the above conclusions and with classification of Warren and Olshausen.⁴ However, because the tubules still retain their shape and general distribution, though filled with tumor cells, surrounded by them and infiltrated by them, all in about the same stage of development, we think these cells may be derived from the same tissue of origin as the seminiferous epithelium. Their arrangement and the special stains suggest them to be of epithelial origin. The interstitial cells are glandular cells and have been shown to be the primary source of androgen,⁶ thus they must be epithelial cells of some type. Though transitory gynecomastia occurred in our case, the histological findings which we have to offer suggest that this tumor may originate from totipotent seminiferous tubule cells.

The report of a Leydig cell tumor of the ovary with virilism by Waugh, Venning, and McEachern¹⁴ further substantiates this idea.

SUMMARY

A case of interstitial tumor cell growth is presented. The patient had definite endocrine changes.

¹³ Bonser, G. and Hawksley, J. *J. Path. & Bact.*, 55, 295, 1943.

¹⁴ Waugh, D., Venning, L. H. and McEachern, D. *J. Clin. Endocrinol.*, 9, 486, 1949.

CYSTO-URETHROGRAMS BEFORE PROSTATECTOMY

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The usefulness of cysto-urethrograms in the preoperative evaluation of patients with bladder neck obstruction is well established. Cystoscopy is the only accurate means of determining the exact configuration of the prostate. However, in an elderly patient cystoscopy is not without its physical and psychic hazards. The patient not infrequently submits to cystoscopy with considerable trepidation either because of prior personal painful experience or narrative from others. The surgeon may be hesitant of possibly activating a quiescent infection, producing a false passage, or initiating severe bleeding. In an effort to defer cystoscopy until the time of operation, yet have some foreknowledge of the prostate and its position, various techniques of cysto-urethrography have been developed as an adjunct to the physical examination.

In 1910, Burkhardt and Floercken¹ suggested the injecting of contrast medium into the lower urinary tract for the purpose of visualizing prostatic enlargement. Since then there have been many variations of their technique. Crabtree and Brodny² have presented an excellent historical survey of the development of cysto-urethrography. In our study skiodan and rayopake were used as the contrast media. Skiodan, introduced in 1931 by Bronner and Schueller³ has proven its value in both intravenous and retrograde urography. Rayopake introduced in 1941 by Rubin⁴ for hysterosalpingography was suggested by Richards⁵ to be "the safest and most efficient urethrographic contrast medium yet produced." Following the suggestion of Sweetser,⁶ cysto-urethrograms are made without removing the indwelling catheter. As suggested by Pearson and Wilson⁷ the balloon of a Foley catheter is filled with skiodan and used as a landmark. It is the purpose of this paper to present a further refinement in the technique of cysto-urethrography. This procedure offers a means of obtaining a more accurate urethrographic picture of the extent and configuration of prostatic hypertrophy than do methods previously described. The size and shape of the median and lateral lobes, the proportions of the intravesical and subvesical gland, and the position of the prostate in relation to the bony landmarks are accurately estimated. These cysto-urethrograms are therefore of definite aid in selecting the particular type of operative procedure.

METHOD

Cysto-urethrograms were made on patients requiring preoperative urethral catheter drainage. For the initial relief of urinary retention a No. 18 Foley

¹ Burkhardt, I. and Floercken, H. *Deut. Ztschr. f. Chir.* 105: 110-115, 1910.

² Crabtree, I. G. and Brodny, M. L. *J. Urol.*, 29: 235, 1933.

³ Bronner, H. and Schueller, T. *Surg. Gynec. & Obst.* 52: 254, 1931.

⁴ Rubin, I. C. *J. Mt. Sinai Hosp.* 7: 479, 1941.

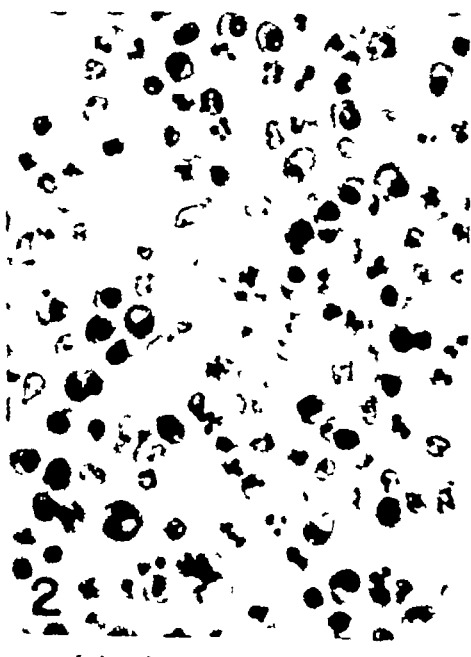
⁵ Richards, C. F. *J. Urol.*, 58: 185, 1947.

⁶ Sweetser, T. H. *J. Urol.*, 40: 285, 1938.

⁷ Pearson, F. I. and Wilson, S. A. *J. Urol.*, 45: 82, 1941.

It did not transilluminate light. The vas deferens was 4 times enlarged. A small cyst on the right epididymis was found. The right testis was normal.

Penicillin therapy was instituted (100,000 units orally every 4 hours for 3 days). The patient returned December 16, 1949 with no regression of the size of the testis. The prostate was firm, nontender, movable and enlarged, grade 1 enlargement. He was admitted to University Hospital. A chest film taken on December 16, 1949, was essentially normal. Film of the abdomen December 20 was essentially normal. The serology was negative. Urinalysis December 19 revealed 100,000 white blood cells and albumin 1 plus. The blood count on December 16 revealed hemoglobin 11.0 gm., red blood cells 3.60 million, white blood cells 7000 differential was normal. The nonprotein nitrogen was 125 mg. per cent.



balloon filled with skiodan rests against the vesical neck, the point of maximum intravesical encroachment of the lateral lobes, or in the sulcus between the median and one lateral lobe. The rayopaque outlines the bulbous, membranous and prostatic urethra. By means of the radiopaque bands in the wall of the

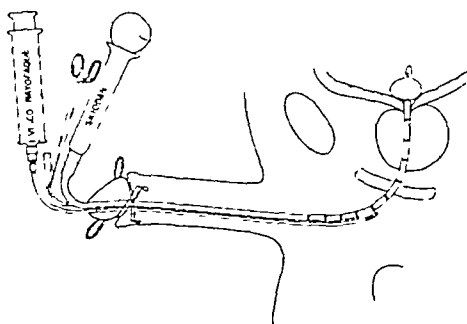


FIG. 2 Diagrammatic representation of catheters in place ready for injection of contrast medium



FIG. 3 F. W. D. II No. B41907 Preoperative cysto urethrogram interpreted as "minimal intravesical, 4 cm. subvesical, 0 median, minimal hypertrophy." Operation: Transurethral resection with removal of 10 gm. tissue.

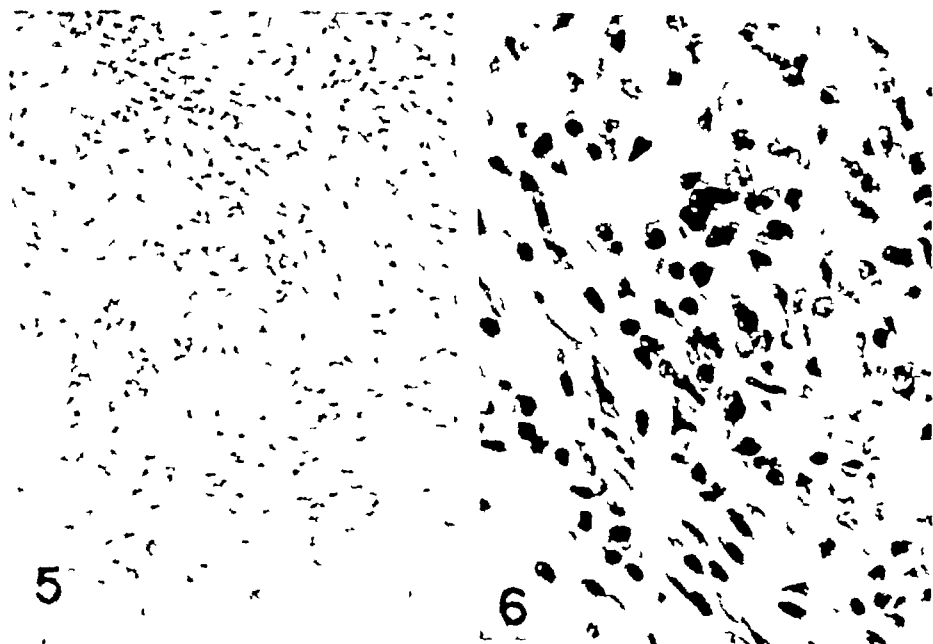
Foley catheter one may measure the dimensions of the prostate. These bands are known to be exactly 1 cm. apart so that no error in measurement due to magnification is introduced.

Except when a large median lobe is present the overall length of the prostate

testis infiltrated by lymphocytes, plasma cells, and eosinophiles. There are seen several foreign body giant cells scattered throughout the section. The tunica albuginea is thickened and the process extends into the epididymis. *Diagnosis:* Carcinoma granuloma testis (fig. 3).

Case 5. A 67-year-old white man was first seen in this clinic with a painless swelling of his left testis which had existed for 4 years.

Physical examination showed a well developed though thin white man who had a left scrotal swelling which was moderately red and indurated. The inguinal lymph nodes were not enlarged and there were no other physical findings of importance.



is measured as the distance between the membranous urethra and the opaque balloon. The distal limit of the prostate is represented by the point at which the rayopaque begins to spread out into the prostatic urethra. The size of the intravesical lateral lobe protrusion is indicated by the distance between the balloon and the distal limit of the vesical shadow. The shape of the prostatic urethra is clearly defined on the oblique film. The size of the median lobe may be estimated by measuring the extent of lateral deviation of the intravesical portion of the catheter.

Measurements of the prostate obtained by this method correspond quite accurately with the dimensions observed at operation (figs 3, 4, 5 and 6). It is

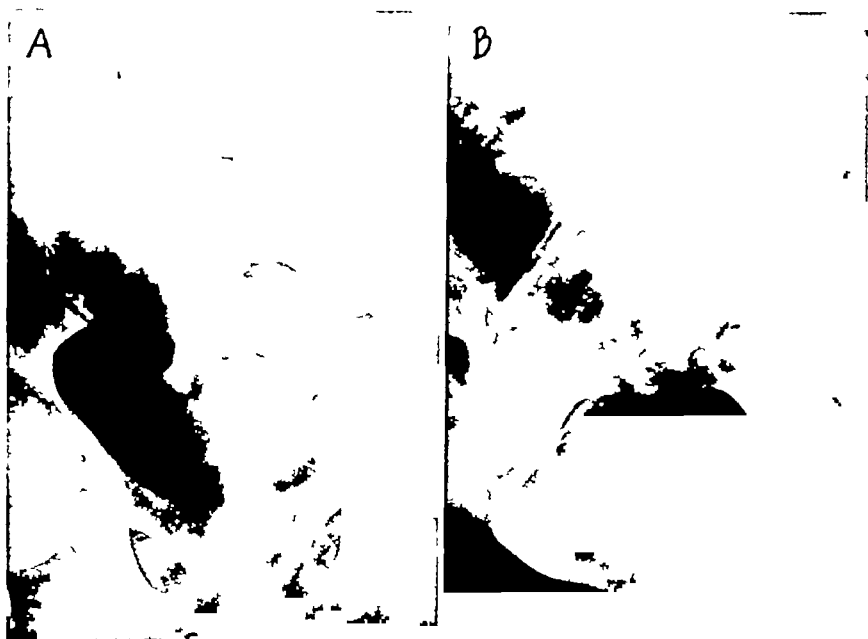


FIG 6 R. L., D. H. No. D2019. Excretory urogram-cystogram showing apparent large intravesical prostatic protrusion. Preoperative cystourethrograms interpreted as '6 cm intra-urethral laterals, very little intravesical gland, almost no median'. Operation: Transurethral resection with removal 30 gm. tissue. No median, minimal intravesical laterals. Gland about $2\frac{1}{2}$ times normal length. Much additional tissue could have been resected.

realized that many factors other than the size and shape of an enlarged prostate are of the utmost importance in selecting the particular type of prostatectomy. The special skill of the individual surgeon, the general physical condition of the patient, obesity, and the nature of associated urinary tract pathology must all be considered. We believe, however, that the measurements have been of help in choosing the type of operation. The small hypertrophy (4-5 cm. overall length) regardless of configuration, is best relieved by transurethral resection. The larger glands (6 cm. up) are perhaps most easily removed by open operation. Retropubic prostatectomy would seem to be ideal for the large intra-urethral gland that projects well above the symphysis pubis. The largely intra-

explanation of the cases is does that of chemico-mechanical irritation of the ureter. It is difficult to see how urine could reach all parts of the seminiferous tubule.

Cases of nonmumps epidemic epididymo-orchitis have been reported in which a general fever preceded the localization in the testis. These cases were unilateral and bilateral. They occurred in armed force personnel. The specific epidemic character of the cases mark them as being different from our cases. They resulted in resolution of the disease in some cases with atrophy of the testis, as far as could be ascertained in other cases.

We are unable to confirm or deny that the present cases may be similar to one previously reported. If they are similar the subject of idiopathic granuloma testis has lacked clear definition. We propose that these cases are important from the standpoint of curing the patient and whether or not surgery may be indicated. They are not to be confused with true tumors of the testis. These cases are marked by unilateral involvement with an insidious onset, lack of severe general clinical symptoms or evidence of sufficient clinical infection to account for the granuloma. The testis was enlarged, hard and fibrotic and heavily infiltrated with chronic inflammatory cells in each case. It is difficult to understand the etiology of the cases. We suspect that many occur and probably there will be a number of agents involved. The use of antibiotics may well be a factor in our case, inasmuch as they easily remove evidence of infection but leave behind a residue to continue damage to the testis. The mechanisms ordinarily advanced for epididymo-orchitis are very inadequate to explain a diffuse unilateral granuloma testis. The spectrum of sensitivity rises here but can neither be aided nor diminished as far as etiology is concerned.

SUMMARY

Five cases of unilateral granuloma testis of unknown etiology are reported. They occurred in healthy white men and were marked by little general symptoms. There was a heavy pain, tenderness, swelling and redness of the scrotum. In one case the swelling showed through the scrotum. Grossly the testis was enlarged and hard and cystic. Microscopically the lesions showed fibrosis and chronic inflammatory cell infiltration. Various etiologic agents are considered but no single causative factor can be predicted.

OSTEITIS PUBIS TREATED WITH ADRENOCORTICOTROPHIC HORMONE

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This report is made because the therapeutically obstinate complication of osteitis pubis has been found to respond favorably to the administration of pituitary adrenocorticotrophic hormone (ACTH). In 2 cases of the acute disease the effect has been dramatic. In 1 case of the chronic disease with complications, improvement also occurred but to a limited degree.

Osteitis pubis is one variety of inflammation of the periosteum, bone, cartilage, and ligamentous structures of the anterior half of the pelvic girdle. Since abscesses and sinuses occur only occasionally, the suggestion has been made that the entity represents a sterile inflammation (secondary invaders producing the occasional purulent manifestations). However, a pre-existing urinary infection is the rule. Furthermore biopsies and cultures made from the involved areas give evidence that the process is microbial even when not grossly pyogenic.¹ Most instances of this disease have followed a suprapubic operation upon the bladder or prostate, but operation is not essential to the pathogenesis as witnessed by a few records of the typical complication following nonoperative disorders, such as pyelonephritis.² The clinical and radiographic manifestations rarely appear in less than ten days following operation, and usually require 2 to 6 weeks. The process typically begins at the symphysis and shows a marked tendency to involve the ischium. Roentgenographically a moth-eaten bony destruction apparently beginning immediately at the symphysis is characteristic in association with evidence of periosteal reaction (spurs and osteophytes) and widening of the cartilagenous space. In the end complete calcification across the symphysis is common. In well-developed cases the patient is incapacitated and suffers with severe pain for many weeks, if not for months. However, the disease is essentially self-limited, fatalities being very rare and in association with additional complications. Spontaneous healing usually provides complete clinical relief but requires several weeks at least. Symptomatic measures such as local heat, physiotherapy, immobilization (even in plaster casts), analgesics, narcotics (addiction is a danger) and general support have been helpful. Therapeutic efforts directed specifically against the pathologic process have usually produced equivocal results, particularly as the improvements have been slow and accordingly possibly due to natural and non-specific factors. Although some of the reports on the use of the new antibiotics are probably overly enthusiastic, the impression remains that benefit does accrue from their use, albeit unpredictable. Of course, with abscess formation, drainage and antibiotics are indicated. Radiation therapy may have helped some patients. Most likely there are many mild instances of this complication which pass nearly unnoticed. For complete clinical subsidence to occur within a week from the

¹ Lavalle, L. L. and Hamm, F. C. *J. Urol.* 66: 418-432, 1951.

² Kleinberg, S. *J. Urol.* 48: 635-641, 1942.

first and a note written 8 hours after the first administration of ACTH stated "Nurses are really amazed as they report that previously they had to give him frequent injections of morphine to relieve his pain and that he had great difficulty in moving around in bed, whereas now he is relatively free from pain." ACTH (100 mg) was given in 5 doses over 24 hours and then discontinued.

For 9½ hours after the last injection of the hormone he remained comfortable without the use of analgesics or narcotics. Then all the previous pain and disability rapidly returned and four doses of morphine 0.15 gm. were necessary in the following 12 hours.

ACTH was again administered in doses of 25 mg. every 6 hours. Again there was prompt and complete relief. Without the patient's knowledge the hormone



FIG. 1. Case 1. A, appearance of symphysis a few days after onset of symptoms of osteitis pubis. B, 2 days later. Note early destruction especially at upper margins of symphysis. C, 5 days after A. Changes now extensive. D, 2 weeks after B, and after ACTH therapy. Note diffuse calcification at upper margin of symphysis.

injections were replaced by similar injections of pure saline. Within 12 hours all clinical signs had returned and morphine every 3 or 4 hours had to be administered as previously.

After 36 hours on saline injections only, and without the slightest relief except from the narcotics and immobilization, the hormone was substituted for the saline without the patient's knowledge. Within 12 hours he again had relief. Forty-eight hours after the first dose of this course of treatment of ACTH, the patient walked to the bathroom, and thereafter remained voluntarily ambulatory.

On the twentieth day after admission progressive elimination of doses was begun and completed on the twenty-third day. In the entire stay in the hospital 875 mg. ACTH was given over 11 days.

abducted passively about 20 degrees without pain and the left leg could be put through an almost completely normal range of motion. In addition, heavy pressure over the symphysis did not elicit tenderness. On the twelfth day of treatment the patient overcame anxiety, got out of bed, and walked in the corridor. The injections of ACTH were progressively stopped between the twelfth and fourteenth day after beginning dosage. A total of 1475 mg ACTH had been administered in 14 days. The pyuria cleared. He was discharged, walking, 5 days after the discontinuance of ACTH. In brief, he came as a stretcher case but walked within 12 days of ACTH therapy without the addition of physiotherapy, radiation, or any antimicrobial drugs. One month later the patient remained free of pain but was weak and apprehensive.

Case 3 S. P., M. H. No. 100551, a 61-year old man, had had a suprapubic prostatectomy performed elsewhere 6 months before admission. The immediate postoperative course had been satisfactory but after 4 weeks a burning pain began in the left ischial region and radiated into both legs. Within a few days he was confined to bed because activity produced severe pain. After admission to



FIG. 2 Case 2. Note evidence of periosteal reaction along ramus.

two hospitals over a 4 months period a slow improvement began but was interrupted by an abrupt recrudescence two weeks previous to referral for trial with ACTH. When admitted he was barely able to walk and complained of severe burning and tenderness about the anterior pelvic girdle and legs. Radiographic examination disclosed bony destruction, calcification, and spur formation of the pubic bones and ischia (fig. 3). The wound was well healed. Five days after admission, no spontaneous improvement being evident, he was given 25 mg ACTH intramuscularly every 6 hours for 8 doses. Even though no objective relief occurred, pure saline was substituted without the patient's knowledge. Within 20 hours the pain was worse and the patient volunteered that although the earlier injections had lessened the discomfort, he was now worse than ever in spite of the supposedly continued treatment. ACTH was then given in the same dosage for 11 days in double dosage for three more days, and finally progressively discontinued over 3 days. A total of 1950 mg was given over 18 days. The pain decreased and the ability to walk increased. However, these benefits were incomplete and appeared slowly. Aureomycin, the passage of a ureteral calculus, ex-

LESIONS OF ISCHIUM AND PUBIS IN PREGNANCY RESEMBLING OSTEITIS

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According to the literature, osteitis of the pelvic bones is a relatively rare condition but extremely so in the female. Only 48 cases have been reported in both sexes, 3 of these are in women. Of the 3 women, one followed a symphysectomy, one followed a traumatic delivery with perforation of the urinary bladder, and one followed pyelonephritis. After having studied the first 2 cases mentioned, little doubt exists that these were true osteomyelitis, as both had sequestra which, when removed, effected cures. Beer found the condition only in those cases in which the bladder had been opened. Marshall, Marchetti and Krantz had 1 case following retropubic urethrovesical suspension that had pain suggesting osteitis.

Some authors believe that the causative factor is a low grade infection, principally the B. coli group of organisms. Others believe the process to be comparable to Sudeck's atrophy. Wheeler had 1 case that came to autopsy showing definite atrophy of cellular elements of bone without inflammatory process of the bone or periosteum. Attempts to reproduce the disease by experiments failed.

Rosenberg and Vest suggest that bone atrophy could be a result of ischemia associated with spasm of blood vessels. Wheeler is of the opinion that osteitis pubis is a result of nerve injury causing an atrophoneurosis.

According to some, the pathological changes are those of fibrous osteitis while others have demonstrated a subacute osteomyelitis in bone curing. Repair occurs by means of an ossifying periostitis and proceeds simultaneously with the lytic stage. It has been stated that it is not unusual to find large spurs despite progression of rarefaction. Ankylosis of the symphysis is not an unusual finding.

The early case may fail to show any x-ray change, the architecture of the involved bones is altered and the trabeculae become somewhat obscured. A fluffiness of the periosteum has also been mentioned. This is rapidly followed by rarefaction which may be spotty or diffuse. Fibrous dysplasia, frank inflammatory process, neoplastic metastasis must be differentiated from osteitis.

Pain begins in the pubis or ischium several weeks to several months following the operative procedure. The pain may be unilateral or bilateral. It may spread to the lower abdomen, perineum or both thighs, depending upon the location of the lesion. Walking or sitting is extremely difficult. Due to spasm of the adductor muscles, abduction of the legs may be painfully difficult. Marked tenderness is present over the body of the ramus of the pubis or ischium. A low grade fever may be present. As a rule the blood count is normal. The prognosis is good but recovery may be delayed for a period of 2 months to 2 years.

Supportive therapy and sedation are agreed upon. Vitamin D and calcium have been suggested. Good results have been reported from x-ray therapy. Opinion

From and of this case and the literature we believe this to be a local interstitial cell tumor.

The microscopic characteristics showed cords and sheets of large polyhedral hyperplastic cells closely resembling interstitial cells which are densely packed between the tubules within the tubules and infiltrating into the connective tissue framework of the tubules without disturbing their structure. These cells filled most throughout the enlarged testis. Scarring of the tubules was minimal.

Distortion of the tubules was absent. The tumor cells appear epithelial in character, stain with eosin and Masson stains.

Gravely the tumor was yellow brown in color and occupied the entire testis.

The patient had transitory gynecomastia for 2 months 9 months prior to operation. The patient made uneventful recovery and is asymptomatic 26 months following treatment.

The case showed evidence that the interstitial cells originate from the same type of origin as the epithelial cells of the seminiferous tubules. To substantiate this statement we offer the special stains suggested the cells to be epithelial. The interstitial cells of the testis have been proven to be the primary source of origin of the glandular cells and consequently epithelial in origin. Therefore, the tumor caused more frequently by interstitial cell tumors than any other type of tumor.

pelvic examination was essentially the same but extreme tenderness was noted over both ischial tuberosities. A bloody vaginal discharge was still present.

May 7, the uterine bleeding persisted. A dilatation and curettage was done obtaining a considerable amount of degenerating decidua.

May 23, the patient returned because of persistent pain. Upon re-examination the pelvic findings were essentially the same but the uterus was smaller and the bleeding had stopped. Exquisite tenderness was elicited upon pressure over both ischial tuberosities. An x-ray was reported by Dr. M. Teitlebaum as follows: "An anteroposterior projection of the entire pelvis including both hips and proximal femurs shows the component bones to be normal in contour, texture, and density, except that there appears to be a superficial erosion of the undersurface of the conjoined rami. The process is symmetrical and in view of the patient's age, cannot be developmental. There is no reaction in the bones or soft tissues. The differential diagnosis lies between a low grade osteitis and a response to abnormal strain with hyperemia and porosis at the muscle insertions. No other abnormality is recognized. It is suggested that the patient be re-examined at short intervals to follow the further course of the process" (fig. 1, B).

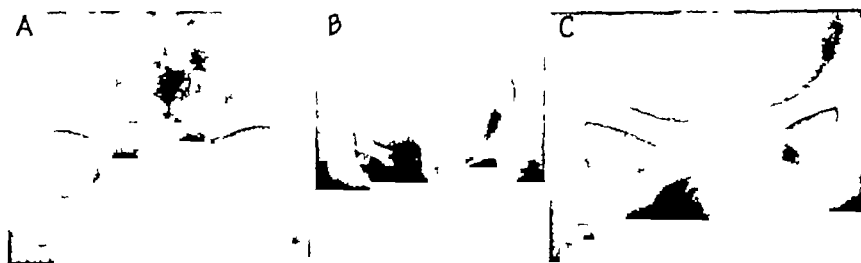


FIG. 2. A taken in Germany in April 1948, showing considerable separation of symphysis and rarefaction of pubis. B taken September 1948, showing essentially same as A but dislocation of symphysis more evident. C, taken January 25, 1950 showing marked improvement of bony structure but still some separation and dislocation of symphysis.

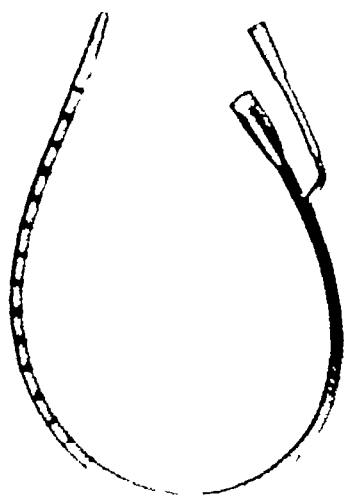
When this information was received the cystogram was again reviewed and the process was found to be present at that time but to a lesser degree.

January 25, 1950, follow-up by mail revealed that the patient recently returned to work as a stenographer but found it somewhat uncomfortable to sit on hard surfaces and continued to walk with difficulty. Follow-up x-rays showed that there had been marked progression of lesion before healing phase had begun (fig. 1, C).

Another patient was seen on January 25, 1950, in the clinic at Touros Infirmary. She was a refugee from Germany and brought with her the x-ray taken there (fig. 2, A and B). She stated that in April 1948, she had a normal delivery with a labor that lasted about an hour. She did however experience great difficulty in walking beginning with the seventh month of her gestation. Three days following delivery she was not able to roll over in bed to enable her to nurse her infant. Abduction of her leg was also difficult. She claims to have had some fever for the first few days but, when forced to remain in bed for a period of five months, and had much difficulty in walking for an additional month. On admission she had only occasional discomfort upon walking.

catheter is inserted. This catheter differs from the standard model only in that the piggy rings have been incorporated into its wall at one centimeter intervals distal to the balloon (fig. 1). During the course of preoperative evaluation cysto-ulithiograms are obtained in the following manner:

- A. The Foley catheter balloon is distended with 5 cc. 40 per cent skiodan.
- B. The catheter pulled down snugly to fit into the vesical orifice.
- C. A No. 10 Robinson catheter is inserted 4 or 5 cm. into the anterior urethra beyond the Foley catheter.
- D. A Zipper clamp is placed around the coronal sulcus.
- E. Sufficient 10 per cent skiodan is introduced through the Foley catheter to distend the bladder just to the point of discomfort.
- F. Rayopaque 20 cc. is then injected through the Robinson catheter.
- G. An anteroposterior x-ray is taken.



AUREOMYCIN IN URINARY TRACT INFECTIONS

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Management of infections of the urinary tract has become increasingly more satisfactory as more effective antibacterial agents are developed. Certain cases, however, fail to respond to specific treatment with any of the substances previously available, even after necessary surgery has been performed. Therefore it is important to investigate thoroughly any new drug which may be suited for use in urinary tract infections.

Aureomycin was early considered in this type of infection because a) it is effective *in vitro* against a variety of gram positive and gram negative bacteria, many of which are common offenders in the urinary tract, b) it may be given for long periods without giving rise to increased bacterial resistance, c) it is eliminated in the urine in an active form and in highly therapeutic concentration, d) it can be administered orally, thus eliminating the need for supervised injections, e) as far as is known it produces no renal damage in moderate doses, f) side reactions are minimal, even when given for extended periods. Moreover, the drug is most active in an acid medium. Because of these properties, a complete study was initiated late in 1948 to determine the precise role of aureomycin in the treatment of urinary tract infections.

Since this work was started, several reports have appeared in the literature which indicate the usefulness of aureomycin in this type of infection. Most of these articles deal with relatively small numbers of cases (Brver et al.,¹ Schoenbach,² Brver and Long,³ Jukes,⁴ Rutenburg and Schweinburg,⁵ Spink and Yow,⁶ Yeager, Beverly and Holbrook,⁷ Brainerd et al.,⁸ Finland, Collins and Paine,⁹ Wilcox and Findlay,¹⁰ LoPresti, Ross and Rubin,¹¹ and others). In addition, Rubin and Goldstein¹² and Rutenburg and Schweinburg¹³ have reported reli-

The aureomycin used was furnished through the courtesy of the Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

We wish to thank Drs. A. C. Posner, Director of Obstetrics, Norman F. Laskey, Chief Urological Division, Department of Surgery, and Solomon Weintraub, Director of Pathology for their co-operation.

*Deceased January 14, 1951.

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⁴ Jukes, R. F. *Ohio State Med. J.*, **45**: 460-461, 1949.

⁵ Rutenburg, A. M. and Schweinburg, F. B. *Proc. Soc. Exper. Biol. & Med.*, **70**: 461-467, 1949.

⁶ Spink, W. W. and Yow, I. M. *J. A. M. A.*, **141**: 964-966, 1949.

⁷ Yeager, G. H., Beverly, W. L. and Holbrook, W. A. *Ann. Surg.*, **130**: 576-588, 1949.

⁸ Brainerd, H., Jennette, I. H., Meiklejohn, G. Bruyn, H. B., Jr. and Clark, W. H. *J. Clin. Invest.*, **28**: 992-1005, 1949.

⁹ Finland, M., Collins, H. S. and Paine, T. F., Jr. *J. A. M. A.*, **138**: 916-919, 1948.

¹⁰ Wilcox, R. R. and Findlay, G. M. *Brit. Med. J.*, **2**: 257, 1949.

¹¹ LoPresti, J. M., Ross, S. and Rubin, M. B. *Pediatrics*, **5**: 734-737, 1950.

¹² Rubin, S. W. and Goldstein, A. E. *Ann. Int. Med.*, **32**: 661-672, 1950.

¹³ Rutenburg, A. M. and Schweinburg, F. B. *New Eng. J. Med.*, **241**: 698-700, 1949.



FIG. 1. J.M.D.H. No. CS 022. Pre-operative cystourethrogram interpreted as 'lateral lobe carcinoma of the prostate gland'. Operation: Suprapubic prostatectomy. Prostate gland 100 gm. Measured mean diameter remainder of gland mass: 6 cm. length, 5 cm. width, 3 cm. depth.



those with insignificant bacteriology or minimal symptomatology. The need for surgery was performed whenever indicated, but with no relation to aureomycin therapy. Some of the cases had resisted previous therapy with sulfonamides or other antibiotics, but this was not a criterion for inclusion in the series. Since the purpose of this study was to evaluate the role of aureomycin *per se*, combination therapy was not employed.

Slightly over 50 per cent of the cases in this series were acute infections (table 1). Most of these occurred in females and the majority were diagnosed as pyelonephritis secondary to pregnancy (table 2). The chief complaints of these pa-

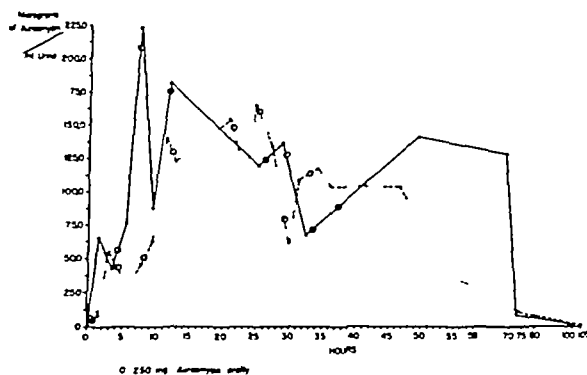


FIG 1 Urine levels of aureomycin following 10 gm orally/day

TABLE 1 Cases of urinary tract infections

TYPE OF CASE	NUMBER OF CASES	STERILIZED BACTERIOLOGICALLY	CURED CLINICALLY*	IMPROVED CLINICALLY†	NOT IMPROVED CLINICALLY	AVERAGE NO. OF DAYS TREATED
Acute	62	36 (58%)	44 (71%)	17 (27.4%)	1 (1.6%)	8
Chronic	51	17 (33.3%)	16 (31.4%)	29 (56.9%)	6 (11.7%)	13.5
Total Cases	113	53 (46.9%)	60 (53.1%)	46 (40.7%)	7 (6.2%)	10.4

* Complete disappearance of signs and symptoms

† Marked reduction of signs and symptoms

tients were costovertebral angle tenderness or pain, pyuria, dysuria, frequency and chills and fever. The remaining cases were of a chronic nature, the majority of the patients being middle-aged or aged males. These cases presented a varying complexity of signs and symptoms including retention (partial or complete) pyuria, dysuria, frequency, urgency, nocturia, hematuria, low back pain, suprapubic tenderness, etc. (table 3). Most of the males had prostatic complication.

Practically all of the patients in this series were hospitalized for surgical or obstetrical reasons and due to the need for bed space many could not be detained for as long a time as might have been desirable. Most of these patients suffered from malnutrition, chronic fatigue, lack of fresh air and poor hygiene. All of

enlarged particularly with a large median lobe is best removed by suprapubic prostatectomy. The perineal approach is ideal for the low lying gland with hypertrophy of the intraurethral lateral lobes.

SUMMARY

A review of the technique of cystourethrography is presented.

Prostate is injected into the urethra alongside a Foley catheter that has been modified by the addition of radiopaque graduations within its wall.

Measurement of the size and nature of prostate enlargement by this means is more accurate than by any other method we have used with the exception of the biopsy.

The measurements obtained are of aid in selecting the type of operative procedure.

Distortion of measurement due to magnification of shadows upon the x-ray film is corrected by means of the opaque graduations lying directly within the prostatic urethra.

The cystoscope used for the measurements is inserted at the time of initial diagnosis and need not be changed until the time of operation.

Grateful acknowledgment is given to Dr. Edwin P. Alvey, Professor of Urology, Duke University School of Medicine, for encouragement and helpful suggestions during the course of this study.

We wish to thank C. R. Paul, Inc., Summit, N. J. for supplying the special catheter and Hoffman-La Roche, Inc., Nutley, N. J. for the rayopaque used in the catheter.

except for a few cases, follow-up examinations were impossible because of the lack of understanding or cooperation on the part of the patients

METHODS

The general procedure in this study was to ascertain first the need for aureomycin therapy on the basis of presenting signs and symptoms and bacteriology of the urine. This need was confirmed when the urine culture was found to be positive. The patient was then given 250 mg. of aureomycin orally four times daily (in most cases) until asymptomatic for 48 hours with a sterile urine, or, in some cases, until it became obvious that the patient was not responding to the drug and was thus a failure. During treatment frequent samples of urine were obtained for culture, in males after careful local preparation and in females after

TABLE 4 *In vitro* sensitivity of microorganisms isolated from the urinary tract

ORGANISM	TOTAL NO. OF CULTURES	NO. SENSITIVE TO LESS THAN 50 Mcg./Cc.					NO. SENSITIVE TO 50-200 Mcg./Cc.					NO. SENSITIVE TO MORE THAN 200 Mcg./Cc.				
		A*	C	P	S	T	A	C	P	S	T	A	C	P	S	T
<i>Escherichia coli</i>	25	24	3	0	0	9	1	18	0	19	12	0	4	25	6	0
<i>Aerobacter aerogenes</i>	15	5	1	0	1	1	9	2	1	6	5	1	12	14	8	0
<i>Proteus</i>	10	0	0	4	0	0	1	3	2	1	1	9	7	4	0	4
<i>Pseudomonas</i>	2	0	0	0	0	0	0	0	0	0	1	2	2	2	2	0
<i>Paracolon bacilli</i>	3	1	0	0	0	0	0	1	0	0	0	2	2	3	3	0
<i>Beta hemolytic streptococcus</i>	9	2	0	4	0	0	2	4	4	1	2	5	5	1	8	4
<i>Streptococcus viridans</i>	6	5	4	6	3	1	0	2	0	2	0	1	0	0	1	0
<i>Non hemolytic streptococcus</i>	4	2	0	3	1	1	1	3	1	0	0	1	1	0	3	0
<i>Staphylococcus albus</i>	24	4	0	5	1	3	0	18	0	20	0	20	6	19	3	6
<i>Staphylococcus aureus</i>	4	3	0	2	0	0	0	2	0	2	0	1	2	2	2	0
<i>Micrococci</i>	5	1	0	3	1	1	0	2	0	2	0	4	3	2	2	1
<i>Yeast cells</i>	3	0	0	0	0	0	0	0	0	0	0	3	3	3	3	—
Totals	110	47	8	27	7	16	14	55	8	53	21	49	47	70	70	15

* A—Aureomycin, C—Chloromycetin, P—Penicillin, S—Streptomycin, T—Terramycin
(Above results are based on a 24 hour incubation period)

thorough cleansing followed by catheterization. In all cases, the first portion of urine passed was discarded. Some of the males had prostatic cultures taken in addition to urine cultures. The criteria for aureomycin discontinuance rested on a bacteriologic and clinical basis. Urinalyses were performed frequently on each patient. All of the bacteria involved in these infections were isolated in pure culture and many of them were submitted to *in vitro* sensitivity tests (table 4). Also, urine and blood levels of aureomycin were determined on some of the patients. Figure 1 shows typical urine levels.

For culture purposes, approximately 15 milliliters of aseptically collected urine was centrifuged at high speeds for 15 minutes. Most of the supernatant fluid was then decanted and the remaining 1-2 milliliters thoroughly suspended. This material was aspirated into a sterile pipette and two drops were streaked on the surface of a blood agar plate and two additional drops on the surface of

one, as has been pointed out by other investigators, but possibly may be avoided or reduced by maintaining the patient on a low residual dosage of aureomycin for several days following the elimination of symptoms.

The majority of the infections in the acute group were due to *Escherichia coli* either alone or in combination with other organisms (table 5). Other organisms occurring frequently were *Aerobacter aerogenes*, *Staphylococcus albus*, micrococci (pleomorphic gram positive cocci in irregular groupings), non-hemolytic streptococci, and anaerobic streptococci. In all, a total of fourteen different bacteria were isolated from acute cases on original culture. A few of these persisted throughout the course of treatment (table 6), but in only 6 acute cases was there no diminution of the original flora (table 2). All other cases showed either a complete disappearance of bacilluria within the course of treatment (58 per cent) or a diminution of the original flora, with or without the develop-

TABLE 6 *Organisms remaining after treatment*

ORGANISM	TOTAL NUMBER OF CASES	PERSISTED THROUGHOUT TREATMENT		OCCURRED DURING OR AFTER TREATMENT	
		Acute	Chronic	Acute	Chronic
<i>Escherichia coli</i>	5	5	0	0	0
<i>Aerobacter aerogenes</i>	6	0	4	2	0
<i>Paracolon bacilli</i>	5	1	2	0	2
<i>Proteus</i>	24	1	9	7	7
<i>Pseudomonas</i>	3	0	1	0	2
<i>Staphylococcus albus</i>	16	3	5	4	4
<i>Staphylococcus aureus</i>	2	0	0	1	1
Micrococci	5	1	1	3	0
Beta hemolytic streptococci	3	1	0	2	0
<i>Streptococcus viridans</i>	3	0	0	1	2
Non hemolytic streptococci	5	0	3	0	5
Anaerobic streptococci	2	0	1	0	1
Diphtheroids	3	1	0	0	2
Yeasts	7	0	0	5	2
Totals	92	13	26	25	28

ment of a resistant secondary flora. The incidence of secondary organisms occurring either during or after treatment is shown in table 6. It will be seen that *Proteus* and yeasts were the commonest offenders in this regard in acute cases and both were quite resistant to aureomycin and other antibiotics (table 4). Most of the other organisms, with the notable exception of residual *Staphylococcus albus*, were either quite sensitive to aureomycin (50 mcg. or less) or moderately sensitive to aureomycin (5 to 20 mcg.). These sensitivity divisions were set up arbitrarily. The apparent discrepancy between clinical and bacteriological results in table 2 may be explained on the basis that some of the 6 cases not responding bacteriologically but responding clinically yielded original cultures consisting of questionable pathogens such as micrococci, diphtheroids, *Staphylococcus albus*, etc. The one clinical failure was caused by an *Escherichia coli* infection which was not eradicated. On the whole, however, there was a good

copy and other urologic measures undoubtedly contributed to the betterment but it was our impression that some improvement had begun before these later events. When discharged 3 days after the last ACTH therapy the improvement in walking was considered marked. Excerpts from the last clinic note of one month after discharge are: Patient looks generally much better. His ability to walk noticeably has improved since admission. Both legs can be abducted to at least 45 degrees. Passive motion of legs causes no distress. He does still complain however of discomfort in the legs below the knee where he has fairly marked tenderness.

Briefly there was a moderate improvement which might reasonably be attributed to the hormonal therapy. However several complicating features obscure the study. Probably the long duration of the disease made treatment with ACTH less effective. On the other hand spontaneous improvement may have been imminent.

Objective studies particularly the total blood eosinophil counts and urinary 17-ketosteroid levels demonstrated in each case that the ACTH was producing a



FIG. 2. Case 3. No visible evidence of periosteal reaction and especially spur formation at the sites of pain.

reasonable physiologic response. Toxic reaction did not occur but it is emphasized that controls were rigid and the treatment periods were brief. Hormonal therapy with ACTH does not lend itself to every-day practice but requires a planned regimen controlled by daily observation and appropriate laboratory check, i.e. blood chlorides, sodium, potassium, sugar and electrocardiogram.

biotic even though the offending organism is quite sensitive. This fact is demonstrated by the one clinical failure in the acute group. In this case *Escherichia coli* was the sole organism isolated over a period of seventeen days from the urine of a patient eight months pregnant. The organism was quite sensitive to aureomycin (table 9), but the patient continued to run a septic course consisting of spiking temperature, back pain, pyuria and general malaise. Apparently some underlying disease was involved in this case which prevented the drug from reaching the focus of infection.

The clinical and bacteriological response in chronic cases was variable but generally less favorable than in the acute cases. The cases were mostly among middle aged or aged individuals with symptoms ranging from moderate to severe. Thirty-eight of the 51 cases were diagnosed as cystitis, urethritis, or prostatitis in varying combinations. The remainder had kidney or testicular involvement (table 3). Most of the chronic cases were of long standing (one to two years or more) and presented surgical as well as other medical problems. The duration

TABLE 9 *Sensitivities of consecutive cultures isolated from the same patient**

DATE	ORGANISM	Mcg./Ml. REQUIRED TO PREVENT VISIBLE GROWTH AT 24 HOURS				
		Aureomycin	Chloromycetin	Penicillin	Streptomycin	Terramycin
2/1/50	<i>E. coli</i>	3.9	7.8	62.5	31.25	7.8
2/2/50	<i>E. coli</i>	3.9	7.8	62.5	31.25	7.8
2/3/50	<i>E. coli</i>	1.95	7.8	62.5	15.6	3.9
2/6/50	<i>E. coli</i>	3.9	7.8	62.5	15.6	7.8
2/8/50	<i>E. coli</i>	3.9	7.8	62.5	15.6	7.8
2/10/50	<i>E. coli</i>	3.9	7.8	62.5	31.25	7.8
2/13/50	<i>E. coli</i>	3.9	7.8	62.5	31.25	7.8
2/15/50	<i>E. coli</i>	3.9	7.8	62.5	15.6	7.8
2/17/50	<i>E. coli</i>	3.9	7.8	62.5	15.6	7.8

* Patient B. R., No. 1421, age 33, sex, female, acute pyelonephritis of pregnancy complicated with uremia.

of treatment in these cases varied but averaged about two weeks. Most of these cases also received 250 mg. of oral aureomycin 4 times daily, but a few of the earliest cases received twice this dosage. Most instances of nausea and vomiting and diarrhea were encountered in this early group, due either to the increased dosage or to early impurities in the drug. Little if any toxicity has been encountered in the last 75 per cent of the patients. The general clinical picture in these patients consisted of a rather prompt (3-5 days) reduction of signs and symptoms (35 per cent became asymptomatic) with a disappearance of pyuria and marked subjective improvement. Approximately 53 per cent of the chronic cases continued to show low-grade symptoms throughout the course of treatment and approximately 12 per cent did not respond clinically.

In contrast to the acute cases, only one-third of the chronic cases yielded sterile urine after treatment. This closely approximates the percentage that became asymptomatic. In fact, in all of the chronic cases there was a very good correlation between bacteriological and clinical response. The distribution of

differs as to the value of traction and hip spicas Sitz baths and diathermy have proven beneficial in several cases Reports indicate that antibiotics and chemotherapy did not alter the course of the disease in any instance when they were used Most authors believe that operative intervention is not indicated

CASE REPORTS

Mr. E. G. aged 26, was seen for the first time on April 2, 1949 Her chief complaint was pain about the perineum and some limitation of motion of the right lower extremity She stated that an abortion was performed by a midwife 2 weeks previously Fever was present for the first few days Gestation was advanced to about 8 to 10 weeks The method used in producing the abortion was not determined

Examination revealed a well developed woman obviously in considerable distress Her temperature was 98.6F and pulse 60 No tenderness was noted upon abdominal examination The pelvic examination revealed much tenderness on the lateral pelvic walls The uterus was slightly enlarged, in good position but tender upon palpation The adnexa were normal in size but tender The



FIG. 1. A, showing osteitis of ischium at time cystogram was made B, showing osteitis of ischium taken 5 weeks after A C, showing healing process but progression of lesion was marked before healing began

cervix was pituitous with blood exuding There was no offensive odor The lower extremities were equal size with no edema They were held flat against the table and abducted There was no tenderness along the saphenous veins and Homan's sign was negative Extreme pain was experienced when the thighs were flexed or rotated and abduction could not be obtained

Urinalysis specific gravity 1.015, negative for albumin and sugar microscopic 1-6 white blood cells no red blood cells per high power field serology, negative sedimentation rate—(Westgren) 45 mm per hour sugar 85 mg per cent nonprotein nitrogen 29 mg per cent red blood cells 3,640,000 white blood cells 8,300 differential, within normal limits

The impression at this time was post-abortion pelvic cellulitis (mild) The patient was placed at bed rest and given sulfadiazine and diathermy daily

On April 12 the patient had urinary incontinence A cystogram done to rule out the possibility of a bladder injury (fig. 1, C) disclosed no loss in bladder continuity The incontinence was probably on a reflex basis as it subsided the following day At that time the patient was placed on hot Sitz baths

By April 20 temporary relief had been obtained from the Sitz baths The

a resistant *Staphylococcus albus*. A two-week course of oral aureomycin produced symptomatic relief with a partial clearing of the pyuria. However, resistant *Staphylococcus albus* was again cultured and treatment was discontinued. As in so many older men, the case was complicated by prostatic hypertrophy with a partial urinary retention. It is apparent, of course, that an antibiotic cannot replace surgery and in those cases requiring surgery the antibiotic can, at best, afford only a temporary relief of symptoms.

Due to the large number of cases in this series, it is impractical to give detailed individual data for each case. Therefore, a typical acute case and a typical chronic case have been selected for detailed presentation. These cases are representative of their respective groups and the case history of each is given below.

Acute case S F, Hospital No 7254, aged 20, a Negress, was 6 months pregnant. On February 4, 1950, she was admitted to Harlem Hospital with acute uterine

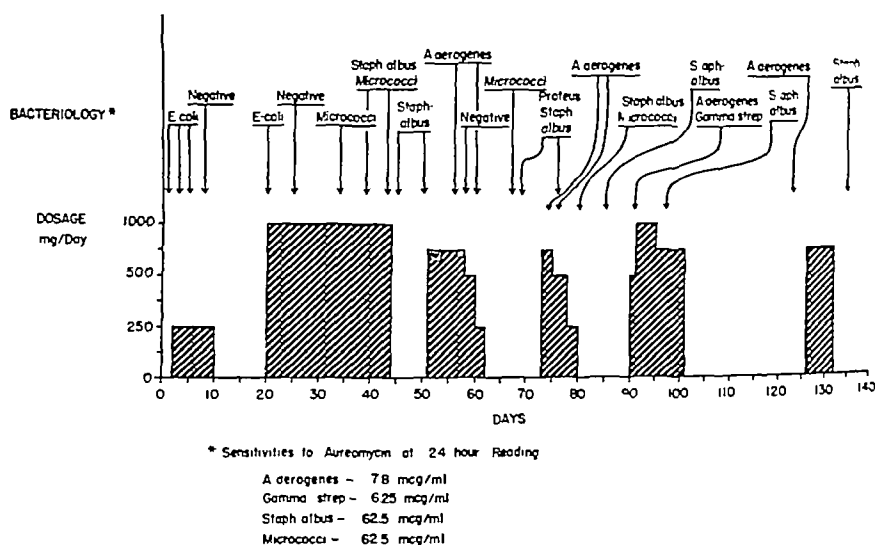


FIG 2 Correlation between dosage schedule and bacteriology of patient L B, treated 4 months

pains and cramps and threatened premature delivery. This acute episode passed uneventfully. On February 9, 1950, chills and a fever of 102.2°F developed with tenderness in the right costovertebral angle. A diagnosis of acute right pyelonephritis was confirmed by pyelography. A urine culture taken on the first day of symptoms revealed numerous *Escherichia coli*. On February 10, 1950, the patient was started on 250 mg of aureomycin orally qid and by February 12, 1950, the temperature was normal and remained normal thereafter. The tenderness was markedly reduced as was the *Escherichia coli* count. By February 14, 1950, all symptoms had disappeared and the urine was sterile. A second culture was sterile on February 15, 1950, and the drug stopped on February 16, 1950, and the patient discharged as cured.

Chronic case H H, Hospital No 18653, aged 65, a Negro, was admitted to Harlem Hospital on October 11, 1949, for chronic urinary symptoms of several

It is interesting to note that the interpretation of the films, taken by Dr Göbb of Bad Tölz, Germany, was tuberculosis. He further stated, that after the patient had been immobilized and the tuberculosis had become less active, a bone graft was indicated. The patient states that there was considerable disagreement among members of the staff. One faction wanted to graft a piece of bone to her symphysis and another stated that the process was one of an abnormal separation of the symphysis associated with a rapid delivery. The operation was refused as the patient wanted to see what the American doctors would have to say. An x-ray of the pelvis at this time is shown (fig 2, C).

CONCLUSIONS

Two cases of osteitis of the pelvic bones are presented, one, osteitis of the ischium following a criminal abortion, and the other, osteitis of the pubis following what appears to be a normal spontaneous delivery. In both cases x-ray evidence is presented.

It is the author's opinion that the condition is not too rare. It is believed that the occasional case in which the patient finds difficulty in walking after parturition is interpreted as a subluxation with separation of the symphysis. Most of these get relief from supports and no further investigation is undertaken. It is the author's opinion that some of these patients, if studied by x-ray, would show findings comparable to the foregoing case reports.

It is difficult to determine from the literature the correct nomenclature. It seems possible that the disease process in question may be divided into two categories, i.e., inflammatory and neurotrophic with the same clinical and roentgenological findings.

I wish to acknowledge the use of the second case from Dr Fishman of the Urological Department of Touro Infirmary and to Dr Pazant, the acting head of the Department of Roentgenology of Touro Infirmary of New Orleans, to Dr Lane, Head of the Department of Roentgenology of the Presbyterian Hospital of Philadelphia, and to Dr Isidore Cohn, Professor of Clinical Surgery, Louisiana State University, Medical School, for their assistance.

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Bacteriological studies revealed a wide variety of organisms involved in the various cases. Perhaps the most significant finding was that streptococci or coliforms or both were involved in almost 87 per cent of all the cases. In general these organisms were quite sensitive to aureomycin, especially when the relatively high urine levels attainable with aureomycin are considered. Almost half of all urines in this study were rendered sterile during the course of treatment (53 patients). Forty-eight patients showed either a disappearance of the original flora with the development of a resistant secondary flora or a quantitative reduction of the original flora with or without the development of a secondary flora. Only 12 patients (slightly over ten per cent) received no bacteriologic benefit.

Proteus organisms proved difficult to eradicate, but they were eliminated from a few cases. This may indicate a variation in sensitivity among various strains. *Pseudomonas* organisms were found infrequently in this series. *Staphylococcus albus* also was quite difficult to remove from the urine and sensitivity studies of many residual strains indicated a relatively high degree of resistance to aureomycin. The true significance of these residual organisms, including *Proteus*, *Pseudomonas*, *Staphylococcus albus*, diphtheroids, yeasts, non-hemolytic streptococci, etc. is difficult to evaluate. Apparently, they may maintain low-grade symptoms, but it is questionable whether they alone could be responsible for acute episodes in the chronic case. Their real importance may be in providing easier entrance or maintenance of more potential pathogens.

In most cases there was a good correlation between bacteriological and clinical response. One was almost the mirror of the other, both in regard to disappearance of flora and symptoms and recurrence of flora and symptoms.

Overall, the acute case presented a simpler, more straightforward clinical and bacteriological problem than did the chronic case and this is reflected in the result of each group as a whole.

CONCLUSIONS

A total of 113 urinary tract infections in adults have been treated with aureomycin. Of these, sixty-two were acute cases and fifty-one were chronic cases.

The average dosage of aureomycin was 250 mg. four times daily administered orally. Toxic side reactions were infrequent and generally of a mild nature.

Of the 62 acute cases, all but one showed either a definite reduction or an elimination of all clinical signs and symptoms, usually within forty-eight hours, and thirty-six of the urines (fifty-eight per cent) were sterilized. The most significant single organism in this group was *Escherichia coli*.

The chronic cases generally presented a more complex clinical and bacteriologic problem than did the acute cases. Of the 51 chronic cases, forty-five (88.2 per cent) were either improved or cured clinically during the course of treatment and seventeen of the urines (33.3 per cent) were sterilized. The duration of treatment in this group averaged around two weeks. The most important single organism in this group was *Aerobacter aerogenes*.

Bacteriologically the most important organisms in the entire series were streptococci and coliforms. These bacteria either alone or in combination ap-

tively small series of 25 and 26 cases respectively. The general findings in all of these studies were that aureomycin produced marked clinical and bacteriological improvement except in cases of *Proteus* or *Pseudomonas* infections. Some recurrences occurred if the medication was discontinued too soon. Many of the cases in these reports had been refractory to other forms of treatment. The dosages used varied from one to three grams per day and toxic manifestations were either absent or were mild and of no serious consequence.

Wilhelm and associates¹⁴ found a high incidence of *Aerobacter aerogenes* infection of the urinary tract (50 of 100 consecutive admissions). Eighty-five per cent of these organisms were resistant to streptomycin, but oral aureomycin produced an excellent immediate response in forty-two of the patients (84 per cent). The incidence of recurrence amounted to 43 per cent, but sterilization of the urine occurred on retreatment. No significant toxicity to aureomycin was seen in any patient and no increased bacterial resistance to the drug developed. Collins and Finland¹⁵ reported a total of sixty-six urinary tract infections treated with oral aureomycin. They obtained good results in acute pyelonephritis and cystitis and less favorable results in chronic cases. Resistant *Proteus* and/or *Pseudomonas* organisms appeared in some of the patients either during or throughout treatment. Finland and co-workers¹⁶ found a possible synergistic action between aureomycin and streptomycin in certain urinary tract infections. Carroll, Allen and Flynn¹⁷ treated 62 cases of urinary tract infections with oral aureomycin. Again favorable results were obtained except in cases of *Proteus* and *Pseudomonas* infections.

Collins and associates¹⁵ studied the urinary excretion of aureomycin following single and multiple doses of the drug. They found that slightly over 10 per cent of the drug was eliminated in the urine following single oral doses of 500 and 750 mg. This has been confirmed by us using a dosage of 250 mg four times daily. In another experiment they found antibiotic activity in the urine for 72 hours and longer following the last dose of drug when given orally, either 250 mg twice daily for 10 days or 500 mg twice daily for 7 days. We have found that following a dosage of 250 mg orally 4 times daily for 2 days a significant urine level, i.e. 50 meg or more per milliliter of urine, did not persist for longer than forty-eight hours following the last dose of drug (fig. 1). Sirota and Saltzman¹⁸ have studied the renal clearance of aureomycin in man and have found that the rate of clearance is influenced solely by the glomerular infiltration rate and the plasma protein binding. They concluded that the urinary concentration of aureomycin in any one individual is directly proportional to the urine flow.

This paper describes our experiences with aureomycin in 113 cases of urinary tract infections in adults. No attempt was made to select cases except to discard

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¹⁸ Collins H. S., Wells L. B., Paine, T. F., Jr. and Finland M. *Proc. Soc. Exper. Biol. & Med.* 69: 174-175, 1948.

¹⁹ Sirota J. H. and Saltzman, A. *Bull. N. Y. Acad. Med.*, 26: 278-279, 1950.

USE OF HELIUM IN PERIRENAL INSUFFLATION PRELIMINARY REPORTS

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The introduction of gaseous media into the perirenal space was first proposed by Carell in 1921. The procedure delineated the renal surface on the x-ray film because of the contrasting shadow cast by the gas. In this way tumors and cysts of the kidney could be visualized. Since the gas also infiltrates around the adrenal gland, both the normal and pathological adrenal can be outlined. This method has been utilized sufficiently, with gratifying results, to establish it as a dependable diagnostic measure.

Various gases have been used successfully. Oxygen, carbon dioxide, and air have been used by many investigators with good results. It is the purpose of this paper to propose still another gaseous medium, namely helium, which we believe to be more effective.

Helium is an inert gas which is colorless, odorless, and tasteless. The diffusibility of any gas depends upon the size of its molecules, the smaller the size of the molecule the more rapid the diffusion of the gas. According to Graham's law, the rate of diffusion of a gas is inversely proportional to the square root of its molecular weight.

Helium has a molecular weight of 4. Oxygen has a molecular weight of 32 and nitrogen 28. It is then evident that helium has a diffusion rate of almost three times that of oxygen or nitrogen. The only gas which has a smaller molecular weight than helium is hydrogen. However, hydrogen has the great disadvantage of being explosive.

Helium has been introduced into other regions of the body without toxic effects (Cleveland and End used this gas in encephalography). The x-rays were satisfactory and the toxic effects were fewer than when other gases were used. E. Rieen found that helium introduced into the human peritoneal cavity was well tolerated. Remders in 1930 employed helium in producing pneumothorax. Barach used a mixture of helium and oxygen in asthmatics to provide greater ease of the passage of the gas through the narrowed bronchioles.

Perirenal helium insufflation was performed by us in 8 cases, without ill effects, and with excellent roentgenographic results. This modality suggested itself in our first case when perirenal air insufflation revealed that the gas had failed to diffuse to the upper pole of the kidney even though the air was seen to be in the proper plane (fig. 1 A). Helium insufflation in the same patient resulted in a rapid spread of the gas to the upper pole of the kidney and across the midline to the contralateral kidney (fig. 1 B). The roentgenograms and laminograms of the succeeding cases were uniformly good and presented an improvement over the previous technique utilizing oxygen and air (fig. 2).

Perirenal insufflation was performed using a pneumothorax apparatus. About 500 cc gas was instilled on each side. We did not hesitate to do bilateral insufflation.

TABLE 2. Summary of data on acute urinary tract infections treated with aureomycin classified according to diagnosis

NO. OF CASES	MALE	FEMALE	DIAGNOSIS	SYMPTOMS AND SIGNS	AVERAGE Oral Daily Dose	No. Days Treated	AVERAGE CLINICAL COURSE AND TOXIC MANIFESTATIONS	CLINICAL RESPONSE			BACTERIOLOGICAL RESPONSE		
								(Cool Symptom free)	(Cool Symptom reduced)	(Cool Urine sterilized)	1 wk*	1 mo*	1 yr (No relapse)
51 (average age 27 yrs)	1	17	Acute pyelonephritis or pyelitis or hydroureterosis (2 cases with cystitis), antepartum or postpartum (5 females not pregnant)	Costovertebral angle pain or tenderness, chills & fever, frequency, pyuria	250 mg four times daily	7-5	Temperature normal in 24-48 hours. Asymptomatic by 3rd or 14th day of treatment. Three patients complained of nausea. No other side effects.	11	9	1	32	11	5
11 (average age 10 yrs)	8	3	Acute cystitis (9 cases). Acute urethritis (1 case). Acute cystitis and urethritis (1 case)	Suprapubic pain and/or tenderness, fever, dysuria, frequency, urgency, pyuria, hematuria in some	250 mg four times daily	10	Temperature normal in 3-5 days. Symptoms subsiding gradually from 2nd on 3rd day on with marked subjective improvement. No side effects.	3	8	0	5	5	1

* Elimination of original flora with resistant secondary flora, or definite decrease in original flora (quantitative and qualitative) with or without resistant secondary flora.

COMMENT

It seemed that the x-ray shadow contrast between the helium and the body tissues was more than accounted for by the more rapid diffusion of the helium. It was for this reason that a simple and somewhat crude experiment was performed. Two small rubber balloons were equally inflated, one with air and the other with helium. These balloons were then submerged in similar containers of skiodan solution of equal concentration. An x-ray was then made of both containers on one film (fig. 3). This film revealed that the helium cast a somewhat darker shadow than the air.

SUMMARY

The use of helium in perineal insufflation is proposed. The advantages of helium over other gases are discussed. As far as we could determine this is the first time that helium was used in perineal insufflation.

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2 (Age 27 & 21)	2	0	Chronic prostatitis and urethral vesiculitis	Pain in groin or testicle pyuria, frequency	250 mg orally q i d	12	Symptoms disappeared in one patient in 7 days and subsided in 7 days in other patient. No toxicity	1	1	0	1	1	0
1 (Age 65)	1	0	Chronic cystitis and urethritis and right pyelonephritis	Suprapubic & right CVA tenderness, frequency, urgency, dysuria, pyuria	250 mg orally q i d	130	Symptoms markedly reduced but returned when drug stopped. Mild nausea on occasion	0	1	0	0	1	0
1 (Age 45)	0	1	Chronic cystitis	Suprapubic tenderness, frequency, urgency, nocturia, dysuria, pyuria	250 mg orally q i d	85	Symptoms disappeared but returned when drug stopped. Mild nausea on occasion	0	1	0	0	1	0
1 (Age 72)	1	0	Chronic cystitis, urethritis, prostatitis, pyelonephritis, hydro-ureter	CVA pain fever, incontinence, frequency, urgency, malaise, pyuria, dysuria	500 mg orally q 4 h	13	Symptoms markedly reduced after 7 days but did not disappear entirely. Nausea, vomiting	0	1	0	0	1	0

* See Table 2

hours by withholding fluids from the evening feeding till the morning of examination. The anteroposterior scout film is followed by the intravenous administration of 10 or 20 cc of 50 per cent neo-iopax. Six to twelve ounces of Coca-Cola are then given during the next 5 minutes. Radiographs are made at 5, 10, 15,

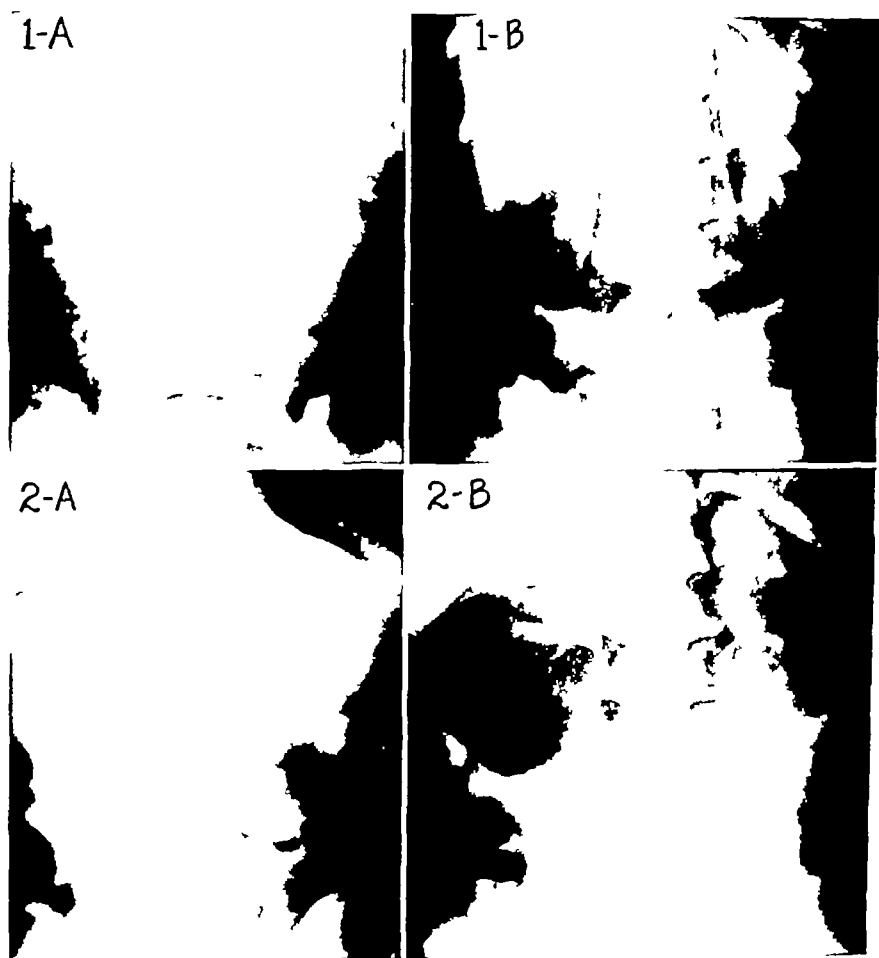


FIG. 1. *A*, K. P., an 8 year old male child. Scout film taken prior to injection of neo-iopax. *1 B* made 15 minutes after intravenous injection of contrast medium, and 10 minutes after ingestion of Coca-Cola.

2, J. B., a 4 year old female child. Made 15 minutes after intravenous injection of neo-iopax, and 10 minutes after ingestion of Coca-Cola.

and 30 minutes after the administration of contrast medium. Older patients have been advised not to eructate. In children under 16 or 18 months, the technique of Matther has been used as originally stated except that neo-iopax has been our preference as a medium.

The use of carbonated beverage instead of milk has greatly improved the soft tissue details of the kidneys and upper psoas shadows. In some instances, the

a MacConkey agar plate. The remaining contents of the pipette were emptied into fluid throglycollate broth (BBL). All cultures were incubated at 37°C for at least 48 hours and any necessary additional procedures were then carried out on the pure cultures thus isolated. All of these procedures were performed directly by us and each sample was cultured immediately after the collection of the urine.

RESULTS

The response in the acute cases was, in general, excellent. In practically each case there was a prompt cessation or reduction of signs and symptoms with a return to normal temperature within 24 to 48 hours. In this group 51 cases were diagnosed as pyelonephritis, pyelitis or hydroureterosis by excretory urography and 11 cases were diagnosed as cystitis or urethritis. In only 1 case was there a

TABLE 5 *Distribution of bacteria in urinary tract infections*

ORGANISM	ACUTE CASES*		CHRONIC CASES*		TOTAL CASES*	
	Number	Per Cent	Number	Per cent	Number	Per Cent
<i>Escherichia coli</i>	28	45.1	9	17.6	37	32.7
<i>Aerobacter aerogenes</i>	8	12.9	22	43.1	30	26.5
<i>Paracolon bacilli</i>	5	8.0	3	5.8	8	7.0
<i>Proteus</i>	3	4.8	13	25.4	16	14.1
<i>Pseudomonas</i>	0	0.0	2	3.9	2	1.7
<i>Bacteroides</i>	2	3.2	1	1.9	3	2.6
<i>Staphylococcus albus</i>	9	14.5	12	23.5	21	18.5
<i>Staphylococcus aureus</i>	0	0.0	1	1.9	1	0.8
Microaerophilic staphylococci	2	3.2	1	1.9	3	2.6
Micrococci	10	16.1	6	11.7	16	14.1
<i>Streptococcus</i>	1	1.6	0	0.0	1	0.8
Beta hemolytic streptococci	3	4.8	6	11.7	9	7.9
<i>Streptococcus viridans</i>	5	8.0	6	11.7	11	9.7
Non hemolytic streptococci	11	17.7	15	29.4	26	23.0
Anaerobic streptococci	10	16.1	3	5.8	13	11.5
Diphtheroids	5	8.0	8	15.6	13	11.5
Yeasts	0	0.0	1	1.9	1	0.8

* 62 acute cases, 51 chronic cases, 113 total cases

negative response clinically, although the group with kidney involvement responded somewhat more readily and more satisfactorily than did the smaller group without kidney involvement (table 2). A few patients who were acutely ill or with hyperemesis gravidans received initial doses of intravenous aureomycin, 500 mg twice daily in an infusion of glucose and distilled water, with no untoward effects. The vast majority, however, received 250 mg of aureomycin orally 4 times daily. Three of the latter patients complained of nausea or morena, but vomiting or diarrhea was not seen in any patient. It was ascertained early in the study that an oral dose in excess of 1 gm daily increased the incidence of side effect without a noticeable alteration of the clinical course. A few cases in the acute group three or four, were readmitted to the hospital 2 to 4 months later with a recurrence of urinary symptoms. The problem of recurrence is a real

We believe Matthei's technique, as originally presented, is the best procedure for infants under 14 to 16 months of age.

In children over 14-16 months of age, the substitution of Coca-Cola for milk has proved to be a useful refinement of the method. It gives excellent soft tissue detail in the upper abdomen and for this reason is helpful in scout films of the abdomen in infants and children even though pyelograms are not indicated.

This type of procedure is well tolerated, is simple and produces greatly improved excretory urograms.

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correlation between the bacteriological and the clinical course. All of the cases in which the urine was sterilized showed a complete remission of symptoms, whereas those in which the original flora was reduced quantitatively showed a lessening of signs and symptoms with general subjective improvement. It is interesting to note that *Pseudomonas* organisms were not isolated from any acute case at any time and of the three *Proteus* infections, two were eliminated during the course of treatment. However, in 7 acute cases cultures yielded *Proteus* either during or after treatment and none of these were eliminated. Despite the secondary flora found in 40 per cent of the acute cases, the patients

TABLE 7 *Division of cases on basis of number of bacterial species involved*

TYPE OF CASE	NO. OF SPECIES PRIOR TO TREATMENT	NUMBER OF CASES	STERILIZED BACTERIOLOGICALLY	PER CENT STERILIZED	CURED OR IMPROVED CLINICALLY	PER CENT CURED OR IMPROVED
Acute	1	29	20	68.9	28	96.5
	2	26	15	57.7	26	100.0
	3	7	1	14.3	7	100.0
Chronic	1	20	9	45.0	19	95.0
	2	11	3	27.2	10	90.9
	3	14	4	28.5	11	78.5
	4	5	1	20.0	4	80.0
	5	1	0	0.0	1	100.0

Total Single Infections 49 with 29 (59.1%) sterilized and 47 (96.3%) cured or improved

Total Mixed Infections 64 with 24 (37.5%) sterilized and 59 (92%) cured or improved

TABLE 8 *Summary of distribution of bacteria in all cases*

TYPE OF CASE	NUMBER OF CASES	TOTAL CASES IN WHICH INVOLVED				
		Streptococci	Coliforms	Streptococci or Coliforms	<i>Proteus</i> or <i>Pseudomonas</i>	Others
Acute	62	29 (46.7%)	38 (61.2%)	54 (87.1%)	3 (4.8%)	19 (30.6%)
Chronic	51	27 (52.9%)	30 (58.8%)	44 (86.2%)	14 (27.4%)	17 (33.3%)
Totals	113	56 (59.0%)	68 (60.1%)	98 (86.7%)	17 (15.0%)	36 (31.8%)

continued to show improvement although not becoming completely asymptomatic. Table 7 shows that of the 62 acute cases twenty-nine were due to a single organism, twenty-six were due to two organisms and seven were due to three organisms. There was a definite correlation between the number of species and the per cent in which sterilization of the urine occurred. Table 8 brings out the fact that streptococci and coliforms were involved in over 87 per cent of the acute cases whereas *Proteus* was involved in less than 5 per cent. This, in part, explains the uniformly good clinical results obtained in the acute cases. It must be emphasized, however, that occasional cases do not respond to a specific anti-

to urologists but with a simple system of filing and cross-indexing of data it is possible to build up an extensive film library. This is of real value in preparing medical papers, and lecturing to students or hospital staffs. This technique is inexpensive compared to any other method and the 35 mm film can be stored in a very small space compared to the original x-ray. A definite advantage is that, from a 35 mm negative, innumerable prints can be made for interested parties (the referring doctor, hospital or office records, and occasionally the patient).

The disadvantages of such a technique is that it is an extra procedure to learn. Each step in photographing film is tricky and time consuming, and unless the individual has some interest in photography it could become a real chore.

COLOR FILM (KODACHROME)

The advantages of using Kodachrome are many. Most important is that when projected it is absolutely grainless, while any black and white film will have some graininess when projected or enlarged. The development of Kodachrome is a positive process which produces a miniature of the original x-ray. There is no doubt that Kodachrome gives better delineation of soft detail than conventional black and white. At times it is possible by experimenting a bit to produce a better reproduction than the original x-ray. Kodachrome is time-conserving compared to black and white since processing is done by factory-trained personnel.

A disadvantage of Kodachrome is that it is more expensive than black and white. Each Kodachrome will cost about 13 cents. It will take the factory from 10 to 21 days to develop and return the Kodachrome film. Air mailing the film saves time but costs slightly more. It is possible there will be a loss of color or "fading" after a period of from 10 to 20 years depending on the method of storing used. However, in the case of Kodachrome copies of x-rays this should not be too much of a problem as there will be only a slight loss in relative black and white or graininess. Another disadvantage is that the individual slide must be projected to be viewed adequately. In the case of black and white the 35 mm negative can be enlarged to 4 by 5 inches which gives a satisfactory size x-ray reproduction.

EQUIPMENT

Any good 35 mm camera is suitable. The author has used the Leica with its many attachments, which makes it an ideal camera. However, the Zeiss Contax, the Argus C-3, the Kodak 35 and other cameras with suitable attachments are satisfactory for this type of work. A 50 mm lens in a collapsible mount makes focusing easier. Some type of ground glass focusing is necessary such as the Leica Focashide. An x-ray view box must be tested with a colorimetric light meter to determine what filter will be necessary for Kodachrome film. The filter may have to be changed if the view box glass is broken or the lights are changed. An upright stand and clamp for the camera, cable release, a light meter and filters will complete the equipment for taking pictures.

For black and white film (Panatomic X was used exclusively) it is necessary to make a print from the miniature 35 mm negative. The resulting print will be a positive but is a "negative" as is the original x-ray itself.

organisms in the chronic cases is shown in table 5. Here we find a preponderance of *Aerobacter aerogenes* with a high incidence of *Proteus*, *Staphylococcus albus* and non-hemolytic streptococci. Again a high incidence of coliforms and streptococci was found (86 per cent) and a relatively high incidence of *Proteus* and *Pseudomonas* (27.4 per cent). The totals for all cases show that streptococci or coliforms were involved in approximately eighty-seven per cent (table 8). Table 6 shows that twice as many organisms persisted throughout treatment in the chronic cases as did in the acute cases. This, of course, is reflected in the poorer clinical results in the chronic group. Only four out of thirteen cases showed elimination of *Proteus* during treatment and one out of two cases showed elimination of *Pseudomonas*. Elimination of an organism in one case and not in another may be due to various reasons, one of which is varying sensitivity from one strain to another. A greater percentage of chronic cases were caused by mixed infections than were acute cases, again one reason for poorer clinical results. However, good correlations were found between the number of species involved, the percentage of urines sterilized and the percentage of cases cured or improved clinically (table 7). It is apparent that the urines of patients with a single infecting organism are more easily sterilized than are those with mixed infections. In general the chronic cases presented a more difficult bacteriological problem than did the acute cases. Sterilization was a more difficult task and in many cases this was due to a slight residuum of the original infecting agents. Also, many secondary invaders were found. In those cases where a slight residual bacilluria of a sensitive organism persisted or reappeared at intervals, the most logical explanation was that a focus of infection was present which was not accessible to the drug. In those cases in which secondary infections appeared, they almost always occurred after the original flora had either been eliminated or markedly reduced. This would indicate either an endogenous infection due to resistant organisms which were present originally in the urinary tract, probably in small numbers, and which came into prominence when the primary flora had been sufficiently altered (a situation analogous to this was found to be true in the intestinal tract after the administration of oral aureomycin²⁰) or an exogenous infection due to "opportunistic" organisms which readily invade and multiply on infected or devitalized tissues.

Recurrence of urinary symptoms is undoubtedly a greater problem in the chronic case than in the acute case. Two of the chronic cases in this series were followed in great detail, one for 85 days and one for 130 days (table 3). In both cases the symptoms and the flora were markedly reduced during treatment only to return to a greater or a lesser extent during the intervals when the treatment was stopped. Figure 2 illustrates the type of bacteriological response that may be expected in the chronic case. The patient, a man 65 years old, was much improved at the end of each treatment period. However, symptoms recurred when the drug was stopped and 6 months after the last course of treatment the patient returned with a recurrence of symptoms and marked pyuria. A short course of oral terramycin proved of no benefit. The only organism cultured was

(Velox) (optional), 6) contact printer (optional), 7) enlarging paper (Kodabromide), 8) a 35 mm enlarger, 9) three 8 by 11 enamel pans, and 10) printing frame

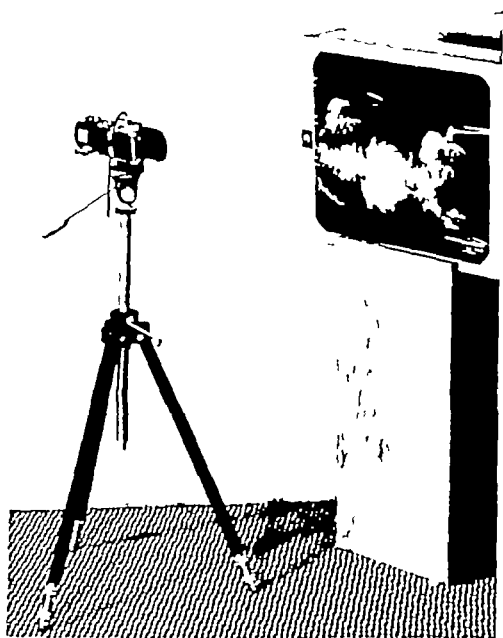


FIG. 3 Less desirable, or alternate horizontal setup

TECHNIQUE

To make 35 mm copies the x-ray to be photographed is mounted on the view box which is best placed on the floor. The camera is then centered over the x-ray by clamping it to an upright stand. By viewing through the ground-glass focusing attachment the lens is moved up or down in its collapsible mount for exact focusing. An additional help is to have the arm that secures the camera to the upright on a movable flange. Any centering or focusing should be done with the diaphragm open to admit the maximum amount of light. A 6 power magnifier placed above the ground-glass viewer will give the finest possible focusing.

It then is necessary to type on thin tissue paper on separate lines the name of the hospital, the x-ray number, the patient's initials (or name if it is not undesirable), age, sex, color, and the date and type of x-ray. Additional help for future reference is the final diagnosis and a brief statement of operative procedure. The author has found that these data can be typed single space on a small slip of tissue paper 3 by 2 inches which can be centered over an unimportant part of of the x-ray such as pelvic bones or lumbar vertebrae. A sheet of carbon paper (with the carbon side toward the back of the tissue paper) gives increased contrast to the typed data. A small L is useful to orient the copy as to right and left, as the edges of the x-ray will not show on the reproduction. A 14 by 17 x-ray reproduces on 35 mm about 11 by 16½ inches when the camera is 25 inches above the x-ray. However, this loss of edge reproduction is not important provided the information is available on the typewritten slip.

years' duration. These included frequency, urgency, nocturia, pyuria, dysuria, suprapubic tenderness. An almost complete retention prior to hospitalization prompted the admission. A diagnosis was made of chronic cystitis and urethritis complicated by prostatic hypertrophy. On October 20, 1949, a suprapubic cystostomy was performed with subsequent urethral dilatation on November 28, 1949 and December 15, 1949. On January 26, 1950, a urine culture revealed *Aerobacter aerogenes*, non-hemolytic streptococci and *Proteus*. A second culture on February 3, 1950, yielded the same three organisms. Aureomycin, 250 mg q.i.d. was given orally beginning on February 3, 1950. During the first week of treatment the symptoms abated somewhat but a culture on February 10, 1950, again showed the same three bacteria. During the second week of treatment all symptoms were markedly reduced, the urine became crystal clear and the patient felt much better subjectively. A resistant *Proteus* infection was the only organism cultured on February 17, 1950 and the drug was discontinued. On March 3, 1950 and March 15, 1950, first and second stage prostatectomies were performed and the patient was discharged on April 4, 1950, as improved. At the time of discharge the patient was able to pass a free stream of urine and the residual urine had been reduced to 150 milliliters. No hematuria was present. The clinical course was afebrile throughout.

The second case history illustrates that the antibiotic afforded the patient relief from his symptoms and at the same time prepared the urinary tract for surgery. As a result of both antibiotic and surgery the patient was markedly benefited and was discharged in a good condition. It is sometimes difficult to evaluate the absolute benefit derived from an antibiotic in the chronic case complicated by surgical needs especially regarding the final outcome of the case. The immediate benefit is more easily ascertained.

DISCUSSION

The clinical response to aureomycin in this series of urinary tract infections was very gratifying. From the overall results it is certain that a valuable aid in the management of urinary tract infections is available in aureomycin. The drug was especially striking in the acute cases probably because most of these cases were simple straightforward problems without much underlying change or surgical complications. However, in the entire series of 113 cases almost 95 per cent of the patients experienced either a substantial reduction in signs and symptoms or a complete disappearance of all signs and symptoms. Even though some of these cases might have recurred after discharge from the hospital (less than half a dozen were readmitted to the hospital with urinary symptoms) the 95 per cent figure is highly significant.

Toxicity to the drug was relatively insignificant. This was probably due in part to the minimal dosage used. In only two or three cases was it necessary to change from oral to intravenous administration because of gastro-intestinal upset and in no case was it necessary to discontinue the drug entirely. From a therapeutic standpoint 10 gm. per day given orally was quite satisfactory. However, it is recommended that the acutely ill patient be given intravenous aureomycin 500 mg. b.i.d. for the first day or two.

the film has dried, strip prints (35 mm size) can be made on Velox paper for a quick survey of photographic technique. This small print can even be placed in a patient's record for future reference if an enlarged print is not desired, or it may be filed with the 35 mm negative to help identify it.

A 4 by 5 inch enlargement on Kodabromide paper is the ideal size. From a 35 mm Panatomic X negative an almost grainless reproduction can be achieved with any good 35 mm enlarger, though the Leitz Focomat is ideal. The smaller the lens f stop, the better the print will be. A certain amount of trial and error is necessary to get good prints unless the individual is an expert photographer. However, it is amazing how quickly one learns this simple technique and how good the x-ray copies turn out. Two years ago the author bought a second-hand Leica with a 50 mm Summar lens and a Leitz enlarger and without previous photographic experience started making x-ray reproductions a year later as an extremely part-time project.

FILING AND STORAGE

Careful labeling of each x-ray film before reproducing it is important. Cross indexing of data is necessary for easy location of any particular black and white negative or Kodachrome slide. Careful handling of 35 mm film is necessary for good projection and prints. Storage in metal containers in a cool dry atmosphere is ideal for both types of film.

SUMMARY AND CONCLUSIONS

The reproduction of all sizes of x-ray on 35 mm film has many advantages: 1) inexpensive, 2) easily stored and filed, 3) permanent film collection, 4) method of recording progress of interesting cases, 5) light weight equipment easily transported, 6) duplicates available for office, hospital, and referring doctors.

The disadvantages of 35 mm film are: 1) small size, 2) initial equipment expensive, 3) slight detail loss from original x-ray, 4) time consuming procedure.

There is a definite place for both black and white (Panatomic X) and Kodachrome. The former makes miniature (35 mm strip prints) and 4 by 5 inch enlargements for office and hospital charts, for referring doctors, and, when indicated, even for the patient himself. Kodachrome makes beautiful lantern slides which are without graininess when projected, and cost only about 13 cents per slide.

The necessary equipment is listed and an easy step by step technique is discussed for taking black and white and Kodachrome copies. Adequate cross indexing of data is mandatory for easy location of slides and negatives.

The author is indebted to Mr. Wayne Eastman, medical photographer of Houston, Texas, for his many helpful suggestions on photographic technique.

The use of Eastman Kodak Company's supplies and E. Leitz Company's equipment does not imply that materials and products made by other companies might not be equally satisfactory.

501 Hermann Professional Bldg. Houston 25, Texas

peared in ninety-eight of the cases (86.7 per cent). Moreover, they are in general quite sensitive to aureomycin. Of the groups that are generally resistant to aureomycin, *Proteus* was found in a high percentage of chronic cases (25 per cent) and resistant *Staphylococcus albus* was found in a large number of secondary infections. *Pseudomonas* occurred infrequently in the entire series.

Of the total cases treated, one hundred and six or 93.8 per cent showed either a clinical improvement or a complete remission of all signs and symptoms. Fifty-three or 46.9 per cent of the urines were sterilized. In general, the acute cases responded sooner and in a more definite manner than did the chronic cases.

PAST PRESIDENT'S ADDRESS Edgar Burns, New Orleans, La

BAILEYER MEMORIAL LECTURE SOME NEW PERSPECTIVES IN RENAL PHYSIOLOGY A A Wolf, Ph D, Albany, N Y

PRELIMINARY PROGRAM, ANNUAL MEETING, MID-ATLANTIC SECTION

AMERICAN UROLOGICAL ASSOCIATION, BELLEVUE-STRATFORD,
PHILADELPHIA, PA, APRIL 17, 18, 19, 1952

UNUSUAL METASTASES OF HYPERNEPHROMA REPORT OF CASE AND REVIEW OF THE LITERATURE Paul Leberman and (by invitation) John J Murphy Philadelphia, Pa

URETERAL PAPILLARY CARCINOMA TREATED BY NEPHRO URETERECTOMY Harry M Burros, Philadelphia, Pa

CANCER OF THE BLADDER TEN YEAR FOLLOW UP OF 122 CASES Col J C Kimbrough, M C and Capt Ferris J Cook, M C Washington, D C

FIBROMA OF THE BLADDER Edward W Campbell, Philadelphia, Pa

METABOLIC STUDIES ON BILATERAL ADRENALECTOMY PATIENTS W W S Butler, John T Grayhack W W Scott and C L Ransom

MALIGNANCY OF THE PENIS A REPORT OF 88 CASES FIRST DIAGNOSED OVER FIVE YEARS Aco John H Furlong Wilmington, Del

TESTIS TUMORS A FIVE YEAR FOLLOW UP Lloyd G Lewis, Washington D C

THE SURGICAL TREATMENT OF VESICOVAGINAL FISTULA Walter I Buchert Danville Pa

TORSION OF THE TESTIS AND HYDATID OF MORCAGNI Robert H Dilcher, Allentown Pa

RETROCAL URETER WITH REPORT OF ONE CASE S L Grossman and (by invitation) John V Fehr, Harrisburg, Pa

CASE OF RETROCAL URETER Francis G Harrison, Philadelphia Pa

A FURTHER STUDY OF PROSTATIC INFARCTION B S Abeshouse and (by invitation) Mino Golden, Baltimore, Md

ACUTE SCROTAL APPENDICITIS Stanford W Mulholland, Philadelphia, Pa

NONOPERATIVE TREATMENT OF STRESS INCONTINENCE IN WOMEN Lawrence R Wharton, Baltimore, Md

PHENOCAPHY A ROENTGENOGRAPHIC STUDY OF THE VENOUS SYSTEM OF THE PROSTATE BLADDER AND PELVIS BY INJECTION OF THE DORSAL VEIN OF THE PENIS B S Abeshouse and (by invitation) Malcolm Ruben, Baltimore, Md

GIANT HYDRONEPHROSIS David M Davis, Philadelphia, Pa

CYSTS OF THE KIDNEY C H deT Shivers Atlantic City N J

CORTISONE THERAPY OF INTERSTITIAL CYSTITIS James F Sullivan, Philadelphia, Pa

CORTISONE IN OSTEITIS PUBIS W J Daw Wilkes Barre, Pa

HORMONAL INFLUENCES ON THE URETER J Mason Hundley, Baltimore, Md

HEMORRHAGIC DISEASE OF (HYPOPROTHROMBINEMIA) INDUCED BY GASTRIN S Miceli and S Keesal and (by invitation) S Silberg and C Bruno



FIG 1 *A*, perirenal air insufflation Laminogram Air has failed to infiltrate region of adrenal and upper pole of kidney *B*, same case as *A* Perirenal helium insufflation (right side only) Laminogram Both adrenal glands clearly delineated

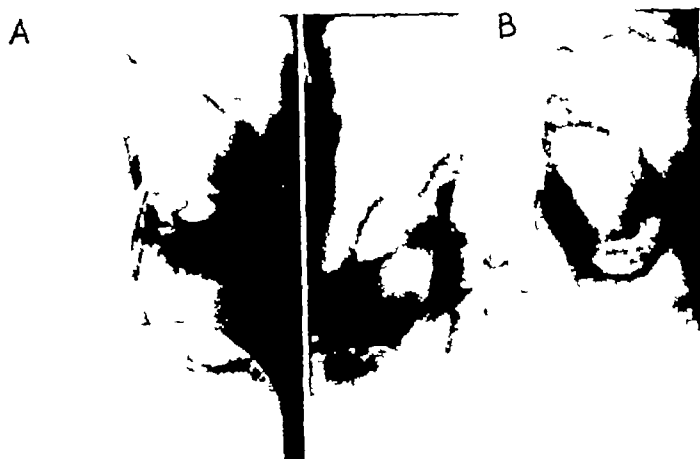


FIG 2 *A*, perirenal helium insufflation combined with retrograde pyelogram Cyst of lower pole of kidney verified by operation *B* bilateral perirenal helium insufflation Simple film



FIG 3 Comparison of contrast shadows cast by helium (H) and air (A) on roentgenogram

tion at one sitting The usual precautions were taken to avoid introduction of the helium into the blood stream The detailed procedure of perirenal insufflation is being deleted since it is now in common use

USE OF CARBONATED BEVERAGE AS AN AID IN PEDIATRIC EXCRETORY UROGRAPHY

OWEN C BERG AND DAVID H ALLEN

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Urological diagnosis in pediatric patients is more difficult and less accurate than in adults, because of the difficulties encountered in the use of the basic diagnostic procedures of cystoscopy, and excretory and retrograde pyelography. The usual preparation and procedure, which in the adult produce diagnostic pyelograms, usually fail to do so in infants and children. This is particularly true of excretory urograms, and the unsatisfactory results have led most urologists and pediatricians to feel that the procedure is of little value.

Recently Matthei¹ has outlined a procedure which will usually produce diagnostic urograms in children. He dehydrates all infants and small children for 12 hours unless specifically contra-indicated. A scout film is taken, after which the contrast medium is injected intramuscularly or intravenously (diodrast). Immediately thereafter, a full 8 ounce bottle of the usual formula is offered the infant, or in the case of the small child, one or more eight ounce glasses of plain or chocolate milk is offered. The ingested material distends the stomach which in turn displaces the colon and small bowel leaving an unobstructed and undistorted view of the kidney structures through the gastric shadow. The administration of a large quantity of milk at the beginning of the examination does not cause sufficient dilution of the dye to interfere with the visualization. He states that the ureters may be obscured, but the method will usually give a good visualization of the pelvis and calyces.

We have used Matthei's technique in several infants and children with good results. It occurred to us that further improvement might follow the use of some medium less dense than milk, since milk approximates unit tissue density and therefore cuts down soft tissue detail. Since the liberation of large volumes of carbon dioxide from ingested carbonated beverages has long been used to distend and study the gastric fundus, it seemed that this would be a satisfactory gaseous medium for distending the stomach during urography. With this in mind, we began substituting Coca-Cola for milk in the Matthei technique. In children over 16 or 18 months this has worked very well. In infants under this age some difficulties have been encountered. While occasional parents object to the use of Coca-Cola, the primary difficulty in the young group has been "bubbling" with the consequent escape of the necessary gaseous medium. This has not been a problem, however, in older children.

It is now our routine to dehydrate all infants and small children for twelve

The authors wish to thank Dr. Norman L. Hemmingway of the Schering Corporation for furnishing the neopax which made this project possible.

¹Matthei, L. P. J. Urol., 64: 417-420, 1950.

SELECTION OF PATIENTS

Two general groups of patients have been approached in this study. In the first group are 9 patients having advanced malignant hypertension with systolic blood pressures ranging from 180 to 250 mm of mercury and diastolic pressures ranging from 120 to 160 mm of mercury. Retinal changes showing hemorrhages and exudate by ophthalmoscopic examination have been present in all. Enlargement of the heart was definite in all, frank cardiac decompensation had occurred in six and previous coronary thrombosis in two. Severe edema from cardiac decompensation had been present in 4 patients. Pulmonary infarction from embolism had occurred previously in 2 patients. Four of this group had definite evidence of renal insufficiency and five showed signs of nephrosclerosis without azotemia. Obvious evidence of cerebral vascular disease had been manifested by five.

In the second group are 5 patients having chronic nephritis as the background of their vascular disease and hypertension. The systolic blood pressure in this group varied from 160 to 240 and the diastolic pressure from 90 to 160. Renal insufficiency was present to a marked degree in four of these and three had severe edema. Vascular changes in the eye grounds were present in all, cardiac and hepatic enlargement were present in four of the five in this group.

In the combined group of 14 patients (9 hypertensives and 5 nephritics with hypertension) 13 bilateral total adrenalectomies have been completed and in one a unilateral adrenalectomy has been carried out thus far. Two of the nephritics have died in renal failure within 3 and 12 days respectively after the second adrenal was removed and one of the hypertensives died of coronary thrombosis 12 days after total adrenalectomy. One patient died of cardiac arrest within an hour after completion of the operation removing the second adrenal gland. Nine of the 13 patients having total adrenalectomy have survived and seven of these have been definitely improved both subjectively and objectively. The other two who were operated upon within the last month cannot yet be judged but one of these has already shown remarkable improvement. In none of these patients has enough time elapsed to determine whether there is any arrest in the progress of the vascular disease but certain definite evidences of circulatory improvement will be described.

PREOPERATIVE PREPARATION FOR TOTAL ADRENALECTOMY

It is naturally preferable to complete the operation in one stage if this can be done with safety. This has been planned and executed in 6 patients successfully (4 hypertensives and 2 nephritics) without a mortality. In 7 patients a two-stage operation was deemed necessary owing to the poor condition of the patient and four of these patients died during the postoperative period as previously mentioned. During the period of preoperative study efforts are directed toward obtaining maximal circulatory efficiency and restoration of cardiac and renal function. A salt-free diet, diminution of edema by diuresis, digitalization and sedation are fundamental in preoperative preparation. Additional measures for correction of renal insufficiency and electrolyte imbalance have been necessary in 4 patients, external dialysis being used for one.

use of Coca-Cola has provided pelvic, and calyceal outlines comparable in quality to retrograde pyelograms. Examples of this procedure are shown in figures 1, 2 and 3.



FIG 2 K E, a 3 1/2 year old male child. A, 8 minutes after intravenous administration of neo-iodipax. B, 15 minutes after intravenous administration of neo-iodipax, and 5 minutes after ingestion of Coca-Cola.



FIG 3 L E, a 11 year old girl. Film made 15 minutes after intravenous administration of neo-iodipax, and 10 minutes after ingestion of Coca-Cola.

SUMMARY

Mutter's procedure for excretory urography has been effective in our hands, and is a distinct advance in the study of the upper urinary tract in infants and children.

left side is usually done first because the left adrenal, being lower, is usually easier to expose than the right, which lies higher and is more inaccessible because of the enlarged liver of these hypertensive patients. The incision is made directly over the twelfth or eleventh rib which is exposed and resected subperiosteally. The subcostal muscles in the rib bed are incised, the lumbodorsal fascia is divided and the false renal capsule opened. Care is taken to avoid opening the pleura in the costovertebral angle. The kidney is partially mobilized and displaced inferiorly, being careful not to exert undue traction on the renal pedicle.

The boundaries of the adrenal are outlined by inspection and palpation. Because of the multiple attachments of sympathetic nerves and blood vessels around the gland's entire periphery, accurate dissection with a wide margin must be carried out. The largest vessels enter and leave the gland superiorly joining the phrenic vessels and inferiorly to join the renal vessels, aorta and vena cava. The vascular attachments are secured with silver clips or ligated after division between hemostats. By dividing the superior and lateral attachments first, a better exposure of the mesial aspect of the gland is obtained. When the gland has been freed laterally and superiorly a rubber covered pulmonary clamp is applied to furnish gentle traction to expose the vessels mesially and inferiorly. Fragmentation of the gland will occur if traction is too great. Adrenalectomy is completed when the inferior vessels have been divided between clamps. On the left side the splenic vessels pursue a course across the operative field and must be avoided in retracting superiorly. The right adrenal may be imbedded in the inferior surface of the liver or in intimate contact with the vena cava. An injury of the vena cava in one patient and of the renal vein in another was controlled by the use of oxidized cellulose gauze. A biopsy of the kidney is made routinely before closing.

If the patient's condition is satisfactory, the right side is opened in the same manner while the closure of the left is being performed. If there have been any clinical findings suggesting pheochromocytoma or cortical adenoma, without localization, a bilateral simultaneous exposure is necessary. If the operation is to be done in two stages a posterolateral exposure is made especially on the right where the gland is usually more inaccessible. In heavy patients removal of the eleventh rib is advisable, particularly on the right side for adequate exposure and facilitation of the operation.

RESULTS

It is not within the scope of this presentation to describe all of the metabolic changes which have been observed after total adrenalectomy. The study was not undertaken with the idea that the adrenal gland is the cause of malignant hypertension, but rather that it is one important factor because of its production of desoxycorticosterone-like substances and that the effects of eliminating the salt-retaining influence deserved investigation. It was fully recognized that most of these patients would not be able to tolerate a drastic fall in blood pressure but that circulatory efficiency might be improved by effective alteration of salt and water metabolism and that possibly an arrest of the progressive vascular

THE REPRODUCTION OF X-RAYS ON 35 MM FILM

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X-rays aid in the diagnosis of many urological diseases. Interesting x-rays are saved for future reference, and in medicolegal cases the preservation of films is most important. In most instances routine x-rays are discarded periodically. However, even the storing of unusual x-rays becomes a problem because of the space required and the inherent danger of x-ray film. Radiologists and others have found the best method of preserving x-rays is to record them on 35 mm film.¹⁻⁹ Siegel⁵ found that a 100 foot roll of 35 mm film makes copies of eight hundred 14 by 17 x-rays and required only 6 cubic inches of space. He found 250,000 copies could be made and stored in a space occupied by only 2000 films in drawer filing. The estimated cost of reproduction in large quantities is from $\frac{1}{2}$ to 3 cents per picture, which includes both master copy and reprint.^{4, 5} However, loss of detail is more or less inevitable in such mass reproductions.

A satisfactory method of reproducing x-rays of all sizes on 35 mm film has been worked out for use by the average urologist with a minimum amount of equipment and expenditure of time. If one is a photographer already, his problem is simple. If he has but casual interest in photography it will surprise him how quickly he will become proficient in copying x-rays. For the novice, x-ray photography will prove interesting and not too complex. Of course, such camera equipment is usable for all types of medical as well as nonscientific photography.

BLACK AND WHITE FILM (PANATOMIC X)

There are many advantages to using 35 mm black and white film (Panatomic X).¹⁰⁻¹⁴ Saving roentgenograms of interesting cases is always a problem.

¹ Hebert, H. L. 35 mm film reproductions of roentgenograms for teaching purposes. *Current Medical Digest*, p. 40, Aug. 1949.

² Nicholas, B. H., and Root, J. C. An improved method for making reproductions from x-ray film. *Radiology*, 27: 362-364, 1936.

³ Root, J. C. Film slide positives on 35 mm film. *The Camera*, 50: 238-241, 1935.

⁴ Malcolmson, P. H. Direct positive microfilm for reproduction of radiographs. *Canad. Med. Assoc. J.*, 46: 68-69, 1942.

⁵ Siegel, A. J. Film filing, the modern way. *Radiology*, 35: 738-741, 1940.

⁶ Busanovich, G. M. The copying of roentgenograms. *Radiology*, 36: 212-216, 1941.

⁷ Aspray, M. Copying of roentgenograms on miniature film. *Am. J. Roentgenol.*, 46: 270-277, 1941.

⁸ Sanderson, S. S. A simplified method of preserving radiographs and allied records on miniature film. *Radiology*, 37: 616-621, 1941.

⁹ Sutherland, C. G. The reproduction of x-rays on films of millimetric dimensions, and suggested potentials of utility in this procedure. *Radiology*, 37: 622-627, 1941.

¹⁰ Turley, H. K. Personal communication.

¹¹ Morgan, W. D., and Lester, H. M. *The Leica Manual*. New York: Morgan and Lester, 1939. pp. 223-235.

¹² Reference Handbook. Eastman Kodak Co., 1948.

¹³ Storage of microfilms, sheet films and prints. Rochester, N. Y.: Eastman Kodak Co., 1946.

¹⁴ Making copies of radiographs. *Radiography and Clinical Photography*, 18: 86-93, 1942.

Only unilateral adrenalectomy has been completed in one of the nephritic group. Nine patients are living after complete adrenalectomy and seven of them are definitely improved both subjectively and objectively. The improvement is attributed to the elimination of desoxycorticosterone-like factors and regulation of its administration as necessary thereafter in such a manner as to avoid excessive retention of sodium and water on the one hand and relative hypotension on the other. It has been shown that absence of the adrenal glands today may be compatible with an active existence owing to available substitution therapy.

ADDENDUM

Since this report was submitted a total of 15 bilateral adrenalectomies for hypertensive vascular disease have been completed. A total of 4 patients have died of cardiac disease and 3 from renal failure. One patient died during an Addisonian crisis the nature of which was not recognized while he was visiting in a distant city. Six of the fifteen are living, five are improved and well, and one is improved but still an invalid because of vascular disease. The presence of severe renal failure is considered an absolute contradiction to total adrenalectomy. A further detailed report of these cases is to be submitted.

This work has been supported in part by funds from the Medical-Surgical Fund, Peter Bent Brigham Hospital, the Eugene Higgins Trust of the Harvard Medical School, the Massachusetts Heart Association, the National Institutes of Health, Public Health Service, and the Ciba Pharmaceutical Company.

The authors are indebted to Dr. Augustus Gibson, Merck and Company, for providing cortisone for this study, to Dr. John R. Mote, Armour Laboratories, for the ACTH used, and to Dr. Harold Hailman, of the Upjohn Company, for aqueous adrenal extract.

The authors also wish to express their gratitude to Dr. Samuel P. Hicks and Dr. Jane C. MacMillan, Department of Pathology, Peter Bent Brigham Hospital for their analysis of the pathological specimens.

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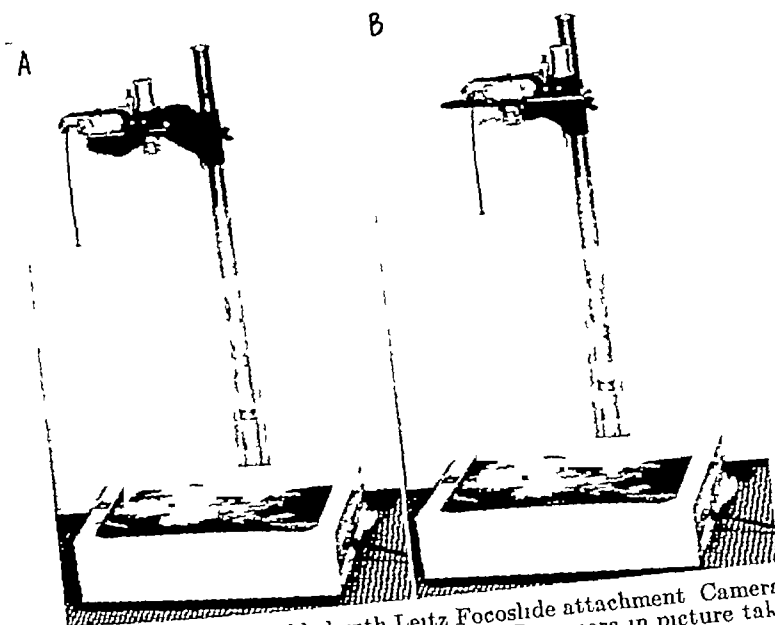


FIG 1 A, Leica camera assembled with Leitz Focoslade attachment Camera in focusing position with 6 power lens over ground-glass viewer B, camera in picture taking position

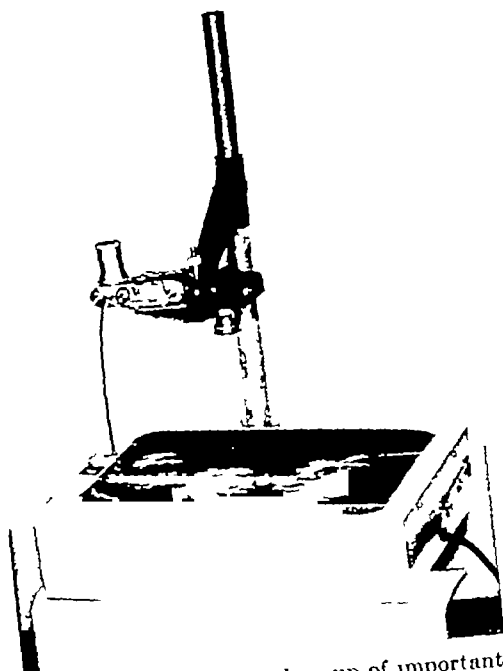


FIG 2 Horizontal arm reversed for close-up of important area of X-ray

See figures 1A, 1B, 2 and 3

The essentials for developing black and white film and making prints are 1) A 35 mm developing tank, 2) Microdol for the film, 3) Dektol for developing the paper print, 4) hypo or acid fixer (for film and paper), 5) contact paper

places to visit these days. One finds there a young team of scholars and investigators and clinicians making discoveries every day, and among these discoveries is that of bilateral adrenalectomy for hypertensive patients, which impressed me the most. This is, of course, a joint adventure between Professors Harrison and Thorn. Dr. Hartwell Harrison, with his customary modesty, has played down the importance of the urological surgeon in this field. It should not be played down, it is very great.

The internist himself, however skilful in the management of hormones and drugs, cannot carry through a successful adrenalectomy in a patient with prostatic cancer, and I give Dr. Harrison great credit for this magnificent study.

I had the great pleasure of seeing some of these people on whom Dr. Harrison had done his adrenalectomies. There were four of them, seated in a room, looking in splendid health. One of the patients, who had previously been bedridden, was now actively engaged as an orderly. There were several Harvard professors also in the room. This orderly was athletic and strong, and despite the presence of these professors he pulled out a package of cigarettes and started smoking, which requires a great deal of audacity in Boston.

Being a congenital optimist and a scientific liberal in what I hope is the best sense of the word—I vote strictly the Republican ticket—I would like to say that I am a little more enthusiastic about this than Dr. Harrison is.

Dr. Harrison emphasized the investigative phases of this study. I think that May 22, 1951 will go down as a great day in American urology.

DR. J. HARTWELL HARRISON: I wish to thank Dr. Cahill and Dr. Huggins for their kindness and their detailed discussions.

It has been necessary in some of these patients for us to do the detailed investigation for pheochromocytoma, using the benzodioxane, palpatory and sedation tests.

I thought it might be worth while to show you the usual operative approach that we have utilized.

(Slide) This illustration shows the prone position of the patient on the table, with the trunk flexed and the lower extremities down about 20 degrees.

(Slide) This shows the position for the bilateral approach to the adrenals, the initial incision being reminiscent of that used by Dr. Young.

(Slide) Here we see the rib exposed; subperiosteal resection is carried out and (slide) the rib bed is exposed. This gives us a small operative field, but in the thin individual it is adequate, in the heavily muscled individual the posterolateral approach must be used on the right side. The right adrenal gland lies much higher than the left. In 4 patients it was imbedded in the liver, and in one it lay on the vena cava.

(Slide) Here we see the superior pole of the kidney brought into view.

(Slide) The kidney is retracted and displaced downward. We see the adrenal gland being brought into view by traction on the renal fascia.

(Slide) That was the left side we just saw. This is the exposure on the right side. We often resect the eleventh rib on the right instead of the twelfth rib.

Small cardboard cut-out arrows placed strategically on the x-ray point out interesting features on the copy. This is especially useful if the original x-ray is under or over exposed.

A reading with a light meter is taken,* using the appropriate Weston index. Panatomic X has an index of 24 but with the green filter in place the film speed becomes 12 Weston. By taking a combined reading over the psoas muscle and the most interesting point of the x-ray, a factor is found which is an index for f stop and time interval. The smaller the aperture (the larger f number) the better the detail and focus, as slight errors in focusing can be overcome in this way. The diaphragm opening and time are set on the camera. The green filter is screwed into place, and making sure that the lens and camera are in apposition (a mistake that is costly in time, and material) the film is exposed by using a cable release. The regular release on the camera may cause jarring and blurring and should not be used.

After photographing in black and white 20 or 36 x-rays (depending on number of exposures in the 35 mm roll) the film is removed from the camera, and a roll of Kodachrome is inserted. The correct Kodachrome filter is attached to the lens and the x-rays rephotographed in the same order. This repeat procedure is much faster since by referring to the notebook, data can be read directly from the light meter, after the appropriate film index is set.

Several helpful aids have been worked out and these include the use of Scotch tape to secure the x-ray to the view box, and a black cardboard mask made by 2 L's. It is advisable to turn the view box light off between exposures (while setting the preliminary factors prior to taking the exposure) as the hot glass causes a slight buckling of the x-ray which makes focusing difficult. Some have used a sheet of glass over the x-ray but this makes for annoying reflections.

One of the most important steps in the whole procedure is to keep a notebook in which to record all data, including the patient's name, hospital number, age, sex, date, x-ray data, light meter reading, f stop and time interval, and filters used. This is a great help in repeating exposures that are unsatisfactory, or when Kodachrome slides are desired. Inevitably, at first, blanks or poor exposures will occur. When a systematic routine is developed adequate reproductions can be made in minimal time. Twenty x-ray reproductions an hour is about an average. This includes typing information, assembling x-rays, and copying the notebook data. Having someone to help out with the clerical work will cut down the time.

PROCESSING

Exposed Kodachrome is sent to the factory for developing. Each exposure is returned in a cardboard readymount which is suitable for projection.

Exposed black and white film is developed either by a commercial photographer (extremely unsatisfactory) or in a light-proof 35 mm tank in Microdol, according to the manufacturer's directions. It is an easy and quick process. When

* Doan¹¹ uses the light meter over the fourth or fifth lumbar vertebra. By referring to a scale he has devised his reproductions all have the same density. This makes for easier printing and enlargements. The author has not used this but it might be helpful.

¹¹ Doan, A. K. Personal communication.

PERINEPHRIC CYSTS

ARTHUR I SPRIGGS

From the Division of Laboratories, Radcliffe Infirmary, Oxford, England

Encysted collections of serous or urine-like fluid surrounding the kidney, although of great rarity, have in the past aroused a good deal of interest and curiosity, and agreement about their origin is still not complete. The occurrence of a case recently (case 2) prompted a review of the subject, which has been given very little attention in English and American journals.

Although some instances of perinephric cysts can be attributed to a previous hemorrhage, or to a perinephric extravasation of urine, others have been found very difficult to explain or to classify, and difficulties of terminology have added to the confusion. Rather than make use of terms such as "perirenal hydronephrosis" (Minkowski 1906), "hydrocele renis" (Krogius 1921), "hygroma perirenalis" (Connerth 1922) and "pararenal pseudohydronephrosis" (Crabtree 1935), it is proposed to speak simply of perinephric cyst, perinephric hematoma and perinephric extravasation of urine, the word perinephric indicating that the process more or less surrounds the kidney. A paranephric cyst, on the other hand, lies alongside the kidney and does not envelop it. Needless to say, cases may arise in which a cystic formation partially surrounds the kidney. Such cases would confound any system of terminology.

Block (1932) gave a full classification of all types of perinephric cysts, abscesses and hematomas. This classification threw blood cysts and serous cysts under one heading, although in some cases all they may have in common is that they are not urinous. It also laid stress on the sub- or extracapsular position of the effusion, which is not always easy to determine, especially as the laminae of the fibrous capsule may be split by collections of fluid. In this paper it is not proposed to adhere to a scheme of this kind, but to deal with the subject under broader headings: 1) perinephric extravasation of urine, 2) perinephric hematoma, 3) perinephric cysts of doubtful origin.

The subject of polycystic disease of the kidney will not be discussed, as it is unlikely that any confusion will arise. Cases in which cysts of the kidney have apparently produced secondary subcapsular collections of fluid are those of Prudden (1885) and Coenen (1911).

PERINEPHRIC EXTRAVASATION OF URINE

As a complication of injuries to the renal pelvis or calyces, extravasation of urine may occur either beneath the fibrous capsule or into the capsular adiposa. In either case encysted collections of fluid may arise, and their distinction in the living subject from true traumatic hydronephrosis may be impossible. These cases are reviewed by Crabtree (1935).

Trauma may precede the appearance of a tumor by many years. An example showing loculation and calcification of the cyst wall was given by Johnson and Smith (1941), the injury had occurred 37 years previously. In old cases, it may

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- BILATERAL HYDRONEPHROSIS AND HYDRO-URETERS THIRD DEGREE RESULTING FROM
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RENAL ANGIOGRAPHY B Marvin Harvard, New Orleans, La
TITLE TO BE ANNOUNCED William J Baker, Chicago, Ill (Guest Speaker)
TREATMENT OF ENCRESIS IN CHILDREN Harold P McDonald, Atlanta, Ga
TITLE TO BE ANNOUNCED Elmer Hess, Erie, Pa (Guest Speaker), President of the American
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URADIAN IN INFECTIONS OF GENITO-URINARY TRACT Charles M Norfleet Jr Parker
R Beamer (by invitation) and Harry M Carpenter (by invitation), Winston-Salem,
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APRIL 4

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E Slotkin, Buffalo, N Y

- CURRENT TUBERCULOUS PROBLEMS IN DAILY UROLOGIC PRACTICE John Dougherty Knoxville,
Tenn
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SOME OBSERVATIONS ON NORMAL AND ABNORMAL BLADDER PHYSIOLOGY Jack Lapides,
Ann Arbor, Mich
VAGINAL TRANSILLUMINATION IN SUPRAPUBIC REPAIR OF VESICOVAGINAL FISTULA E Clay
Shaw, Miami, Fla
TREATMENT OF CARCINOMA OF PROSTATE Rubin H Flocks, Iowa City, Iowa (Guest
Speaker)
PERI URETEROPELVIC CYST Jack Hyman, Mobile, Ala

APRIL 5

- THE SURGICAL TREATMENT OF PROSTATIC CALCULOSIS Truett H Frazier, Orlando, Fla
TOTAL ADRENALECTOMY FOR METASTATIC PROSTATIC CARCINOMA Peter L Scardino,
Charles L Prince and Thomas A McGoldrick (by invitation), Savannah, Ga
THE INDICATIONS FOR URETERO INTESTINAL ANASTOMOSIS Chester A Fort, Atlanta, Ga
UPPER TRIL INJURIES IN GYNECOLOGICAL SURGERY Eugene C St Martin, Burdette E
Trichel and James H Campbell (by invitation) Shreveport, La
IRITRITIC PLASTICS Samuel A Vest, Charlottesville, Va (Guest Speaker)
EVALUATION OF CONTINUED STREPTOMYCIN IN RESISTANT TUBERCULOSIS PATIENTS Thomas
R Huffines Asheville, N C

intrarenal) Out of these, 26 were without discoverable causes, the rest were due to aneurysms, tumors, blood diseases etc More recent reviews are those of Kuysen (1939) and Lesieur (1941), and Ekman (1946) discusses the cases from the point of view of x-ray diagnosis of renal displacement The bleeding is most commonly acute, but may be chronic or relapsing and in these cases can produce a variety of appearances depending on the degree of inflammation, of fibrosis, and of destruction of the capsula adiposa The perinephric fat may show streaks and layers of blood clot, so that it resembles certain kinds of German sausage When fibrosis is advanced, the kidney may lie encased in an armour (Gewebspanzer) of fibrofatty tissue (Kummell 1914), and foci of old hemorrhage may be found within it (Lehnert 1914) On the other hand, encapsulation may occur, and the blood be partially or completely replaced by clear fluid It is this end result which is the main subject of discussion here

Encysted hematoma Mas (1878), 11 days after an experimental crush injury of the kidney of a cat, found what he called an "apoplectic cyst," an elevation of the fibrous capsule from the surface of the kidney by a collection of yellowish fluid, with evidence around it of subcapsular hemorrhage

Hildebrand (1895) described a spontaneous 3 weeks' old hematoma with encapsulation, from a girl of 19, and in this case the fluid was hemorrhagic He (Hildebrand 1924) later saw a traumatic case of 4 months' standing in a man of 37, and the sac contained yellowish watery fluid At operation 2-3 litres were evacuated from the partially loculated perinephric cavity

Koch (1909) reported a case of bilateral spontaneous perinephric hematoma in a man aged 31 At autopsy the cyst on the left side, dating from attacks of pain and swelling in the loin 1 year before, contained serous fluid and some old clot, its wall was 3-8 mm thick The right sided cyst (clinically more recent) contained bloodstained fluid and clot, and its wall was 2 mm thick These cysts surrounded their respective kidneys, and were about the "size of loaves of bread" The kidneys appeared intact and were covered by their fibrous capsules, but the patient had died in uremia, and microscopy showed hyalinization of glomeruli and other changes interpreted as "interstitial nephritis" The capsula adiposa on both sides had disappeared

Color drawings of these specimens were published in Coenen's (1910) paper, and are reproduced here (fig 1)

Balo's (1925) fourth case falls into the same group There was 2 months' history of pain and tumor, and a subcapsular cyst was found covering only the lower pole of the kidney, and containing brownish turbid fluid

Iepoutre (1934) described the case of a child aged 18 months, in which a unilateral perinephric cyst developed 6 months after trauma The child died after nephrectomy The cyst contained viscous fluid of a reddish grey color and its internal surface was partly covered by endothelium and partly showed organizing clot It appeared to have developed intracapsularly on the posterior superior aspect of the kidney, and the kidney substance was compressed Although the author regarded this as a cystic lymphangioma a comparison with other recorded cases justifies its insertion into the post-hemorrhagic category

ERRATUM

Addendum on p 499, October 1951 issue should read
Urine was still negative June 1951

proposes a "perinephritis haemorrhagica capsularis," by analogy with "perimenigitis haemorrhagica." The "capsularis" is put in to emphasise that the kidney itself is unharmed. Other authors maintain that the condition is hardly found except where the kidney is abnormal.

An important cause of perinephric hematoma is renal congestion. Out of 22 dogs whose left renal vein was tied off, Polkey and Vynalek (1933) found some degree of perinephric hematoma in sixteen, in addition to hemorrhages in the parenchyma. Of these, some were subcapsular extravasations, while in others the capsule was ruptured. These authors trace a large proportion of the recorded hemorrhages to sudden congestion of the kidney.

Similar findings have been reported by other workers in renal vein occlusion experiments (Buchwald and Litten 1876, Pawlicki 1906), and perinephric bleeding has been noted in naturally occurring renal vein thrombosis in man (Abeshouse 1945, Barenberg et al 1941), although this is by no means a constant finding. Obviously venous congestion cannot be the sole cause, as many cases of spontaneous perinephric hematoma have shown no congestion, and the disease is not apparently a complication of congestive cardiac failure, in which severe renal congestion commonly occurs, nor of caval thrombosis.

There is one report of a frank perinephric hematoma in a case of polycythemia vera, that of MacKenzie (1930). It contained about a quart of blood and was thought to be extracapsular. The red cell count was 7,800,000 per cu mm.

PERINEPHRIC CYSTS OF DOUBTFUL ORIGIN

Hydronephrosis and serous perinephric effusions. In the majority of cases of nonurinous perinephric cysts recorded in the literature, dilatation of the renal pelvis has been found. In the adult the case has usually been one of malignant obstruction of one or both ureters. Other examples are from newborn children with congenital ureteric obstruction. The cysts are usually interpreted as sequelae of perinephric bleeding, but it should be noted that reports of frank hematoma around a hydronephrotic kidney (except as a result of gross trauma) are even fewer than those of perinephric cysts.

All the cases found are tabulated in table 1 including those of organizing hematoma in which replacement by serous fluid is proceeding, but not yet complete.

Cases in which the fluid is known to be urine, such as Fergusson's (1944) are not included, but this is not intended to imply that all cases tabulated are proved to be nonurinous. Their origin will be discussed later.

The case of Müller (1926) deserves a fuller description since it shows very unusual features. A man of 65, later found to have carcinoma of the rectum, with extensive involvement of the pelvic organs, complained of swelling and pain in the loin of 6 weeks' duration. At operation the fibrous capsule of the kidney was found to be represented by a layer of cysts about $\frac{1}{2}$ cm. thick, enclosing two larger cysts, each of about 200 cc capacity. They contained clear fluid. The cysts had no endothelial lining. Unfortunately, only a restricted post-mortem examination was allowed, but the renal pelvis was found to be dilated, and the cortex much reduced. The author considers lymph stasis and probably inflammation as the causes, rather than hemorrhage.

A STUDY OF BILATERAL TOTAL ADRENALECTOMY IN MALIGNANT HYPERTENSION AND CHRONIC NEPHRITIS PRELIMINARY REPORT

J HARTWELL HARRISON, GEORGE W THORN AND
MODESTINO G CRISCITIELLO

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of Surgery and Medicine of the Harvard Medical School, Boston, Mass*

A study of the effects of bilateral adrenalectomy in malignant hypertension was prompted by a number of factors. First, the possibility of undertaking such a venture was realized because of the availability of cortisone, desoxycorticosterone acetate and whole adrenal cortical extract. The experience of one of us with two patients having hypertension who subsequently developed Addison's disease and became normotensive was the initial specific indication for pursuing such a course of investigation. When one of these patients was given desoxycorticosterone in ample dosage he again became hypertensive and returned to a normotensive state with minimal dosage of this substance. The necessity of and benefit from the salt-free diet in the management of hypertension has long been recognized. The sodium-retaining effects of desoxycorticosterone are well known. In view of the failure of medical and surgical therapy now utilized to arrest the progress of malignant vascular disease in such a high percentage of cases, it was decided to study the physiological changes which bilateral complete adrenalectomy might induce in a small group of selected patients who had failed to respond to strict medical treatment and who at the same time were considered too far advanced to hope for benefit from sympathectomy. By total adrenalectomy it was planned to eliminate as far as possible the salt-retaining hypertensive factors of the adrenal, desoxycorticosterone-like substances, and to attempt to modify the cortisone-DOCA substitution ratio thereafter for the individual patient in proportions compatible with an active sedentary existence and at the same time avoiding salt and water retention.

In embarking on such an investigation it was deemed necessary to choose patients whose prognosis was poor and whose life expectancy with present methods of treatment seemed definitely limited to months rather than years. The implication of this selection is that of patients having irreversible vascular changes involving heart, brain or kidney. The first patient, a man aged 47 years, had such involvement in all three systems mentioned above. He died unexpectedly and suddenly of a coronary thrombosis 12 days after removal of the second adrenal but without having shown any symptoms or signs of adrenal insufficiency. It was learned from this patient that the operation and immediate post-operative period could be successfully conducted with modern substitution therapy and that unpredicted vascular accidents must be expected to occur even after the period of greatest stress has been passed. During the last 10 months 13 bilateral total adrenalectomies have been completed and one adrenal has been removed from two more patients as a first stage procedure.

Read at annual meeting, American Urological Association, Chicago, Ill., May 22, 1951

exceedingly rare, the earliest stages are easily overlooked and may be more common than we suspect. An example of partial elevation of the capsule of a hydronephrotic kidney by brownish-yellow fluid, involving the lower pole only, is given by Balo (1925, third case). A similar picture was recently seen at post-mortem here.

Case 1 Post-mortem 28/1948. Male aged 71, carcinoma of bladder. At post-mortem examination the walls of the bladder were found to be infiltrated throughout by growth and the ureters and kidney pelvis were dilated on both sides (fig. 2). On the left, the capsule was stripped from the upper pole of the kidney over an area 5-6 cm. in diameter, and the space filled with clear fluid forming a shallow cyst. This cyst extended medially to the pelvis, but did not communicate with it. At its margins, the cyst contained a debris of fibrin and blood clot.

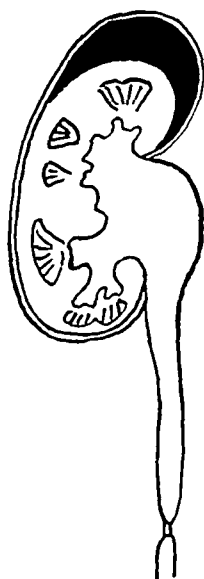


FIG. 2

Histology of left kidney. The capsule shows fibrous thickening, and a few small infiltrations of lymphocytes. The kidney shows arteriosclerosis and moderate sclerosis of glomeruli, with a fairly profuse lymphocytic infiltration of the interstitial tissue. The tubules are variably dilated. The cortex is covered by only the finest layer of connective tissue. At the angle where the fibrous capsule leaves the surface of the kidney, there are some dilated lymphatics and masses of slightly laminated hyaline material, probably representing coagulated protein. The capillaries of the area are congested (fig. 3).

Serous perinephric cysts without hydronephrosis. Perinephric cysts not falling into the categories already dealt with have only very rarely been reported. There has been some confusion caused by paranephric cysts (arising outside the kidney but not surrounding it), being referred to under the same heading or even by the same name. The distinction is in any case artificial, as a cyst may lie beside the kidney, partially surround it, or enclose it completely like a hydrocele.

For simultaneous bilateral total adrenalectomy preparations must be made for adequate hormonal substitution therapy. Cortisone, 100 mg, is given intramuscularly the night before operation and repeated the next morning before surgery. Continuous spinal anesthesia has been safer in these severe malignant hypertensive patients but intratracheal ether makes a better exposure possible. During operation aqueous adrenal cortical extract 100–200 cc and neosynephrin 20–50 mg by intravenous drip is given as required for circulatory stability. Cortisone, 50 mg every 6 hours, is given intramuscularly during the first 48 hours of the postoperative period and this is gradually reduced to 37–25 mg per day as a maintenance dose. A sodium chloride diuresis occurs usually in the first 10 days after operation, but the time of onset of this has varied in different patients. In the late postoperative care salt depletion must be avoided by adding 3+ gm sodium chloride to the diet and/or desoxycorticosterone acetate 1 mgm per day 3 to 6 times a week as necessary to avoid weakness and hypotension from salt depletion. Five of our patients are receiving desoxycorticosterone acetate and four are not. The demands of the individual patient have varied considerably and must be carefully studied and followed over a period of months in order to attain the best adjustment possible.

The hormonal preparation for an unilateral adrenalectomy is the same as for the bilateral operation because the latter is planned to be done whenever the patient's condition will permit. The preparation for the second stage is also similar to that outlined for the single bilateral operation. This substitution therapy has been shown to be adequate to sustain life under the circumstances of an active though sedentary existence. One patient previously incapacitated for 3 years has now been working for 6 months since bilateral total adrenalectomy as a hospital orderly and another has resumed his work as an insurance agent.

The Surgical Approach to Bilateral Adrenalectomy

The surgery of the adrenal gland has been greatly facilitated by the contributions of Young, Crile, Cahill, DeCourcy and Girgloff. The simultaneous bilateral exposure of both adrenals by the posterior approach as described by Young has been valuable in the exploration of patients suspected of having a primary neoplasm of the adrenal, especially when preoperative localization of the tumor has not been established. Subtotal adrenalectomy has been utilized to a limited extent in Cushing's disease. Bilateral total adrenalectomy for reactivated cancer of the prostate was first performed by Huggins and Scott in 1945. Green, Nelson et al reported bilateral subtotal adrenalectomy for malignant hypertension and diabetes in October 1950. We have used the posterior approach chiefly because it confers possible bilaterality to the operation and because the position is well adapted to continuous spinal anesthesia. A posterolateral approach to the right adrenal especially has been used in selected cases.

The patient is placed in the prone position, flexed at the trunk, with the thighs lowered about 20°. This angle is increased in the obese patients. Every effort is made to insure that the patient's position is comfortable and that there is no abdominal compression causing interference with respiration. The

sanguineous fluid every 4-5 days. At operation (nephrectomy), the kidney lay like a testicle in a hydrocele sac, apparently unharmed. The fibrous capsule covered the kidney as usual. Microscopically, the kidney showed "chronic interstitial nephritis," and there was evidence of hemorrhage in the walls of the sac.

The case of Kirmisson (1899) may have been of the same type but the record is incomplete.

Minkowski (1906) published a full account of a perinephric cyst in a man of 21 with polycythemia (R B C 8,500,000, Hb 170 per cent), and possibly congenital heart disease (he had been cyanosed as a child). His complaint was of pain and swelling in the right hypochondrium. Besides a large palpable mass in the right flank, the spleen was thought to be enlarged. Fluid was aspirated from the cyst on many occasions, and experiments (such as taking samples of cyst fluid and of urine after ingestion of methylene blue) proved that the fluid was not secreted by the kidney. At operation the cyst wall was found to be translucent and the kidney lay in its depths, like a testis in a hydrocele. This cyst wall was considered to be the original fibrous capsule of the kidney. There was a very fragile membrane covering the renal cortex. Microscopically, the parenchyma showed a few small foci of hemorrhage, and the cyst wall had no endothelial lining. In Minkowski's view, the effusion was of lymphatic origin, and due to renal congestion.

Krogus (1921) (second case) described the case of a man of 55, with a perinephric cyst on the left side the size of a man's head, full of clear yellow fluid. The kidney was covered by a thin easily stripped capsule, and showed "disseminated interstitial nephritis." The sac had no endothelial lining. Examining the angle of reflexion of the cyst wall, the author found that the capsule was continued as the cyst wall, the kidney being covered by a newly-formed membrane, in which there were hemorrhagic areas. Infection was thought to be a causal factor.

The case of *Rennen (1923)*, that of a man aged 20, showed almost identical features. The history was of 6 weeks' recurrent pain in the left side, with a tumor fluctuating in size. The fluid was pale yellow. The hemoglobin in this case was 105 per cent and red blood cells 5,832,000, and the author discusses polycythemia as an etiological factor. He states that at operation on a polycythemic he has seen the renal capsule cut, and the kidney pop out in a way that indicated clearly its increased vascularity.

The case of *Löffler (1927)* will be referred to in some detail, as it corresponds very closely with our own case to be described shortly (case 2, p. 423).

Female aged 13. Since age of 6 months known to have congenital heart disease. Blue even at rest, clubbing of fingers. At age of 9 had 10,560,000 red blood cells per cu mm and 120 per cent hemoglobin. Developed congestive cardiac failure and died aged 13.

Post-mortem. Heart grossly enlarged. Auricular and ventricular septal defects and severe pulmonary stenosis. Endocarditis of all valves, occluding pulmonary artery.

Capsule of left kidney was separated off anterior surface of kidney over about half its width, by dark purple clot. Around this were several other little cavities.

disease might be attained to give prolongation of a more productive and comfortable existence. The former result has been obtained and the latter will be adjudged by the studies of the subsequent course of these patients.

The subjective symptomatic relief has been carefully studied. There is consistently a great psychologic stimulus as a result of the realization of having successfully gone through the operation. A transitory state of euphoria may be attributed to the temporary administration of more cortisone than is necessary but the continuation of this state of mind after cortisone has been diminished to a maintenance dose, supplying only the daily bodily requirement, indicates that other changes have occurred to contribute to this apparent state of well-being. Specific symptoms which have been relieved are headache, weakness, palpitation, substernal oppression, orthopnea, dyspnea, ascites and edema of the extremities. There has been a notable disappearance of anxiety in most cases. The accompanying clinical signs which account for this symptomatic improvement have been a striking decrease in heart size, clearing of lung fields, increase of vital capacity, diminution in hepatic enlargement, improved exercise tolerance and loss of edema. Concomitantly there has been an accompanying loss of weight owing to a sustained diuresis of sodium chloride and water. Really significant drops in blood pressure with excellent toleration have occurred in four of the 9 patients surviving the total treatment. Three other patients showed moderate improvement of blood pressure with adequate tolerance and two showed no essential change in blood pressure, owing we believe, to the necessity of its maintenance in order to render adequate peripheral circulation through the available vascular bed. Thus far in our observations made over a period of 1 to 7 months after total adrenalectomy no striking changes in the eye grounds have yet been observed. Azotemia previously existent has not in any case been improved as a result of adrenalectomy and the presence of such degree of renal insufficiency as to yield a blood urea level of 50 mg per cent and over is considered an absolute contra-indication to the procedure.

The use of the 8-hour intravenous ACTH test for its effect on the number of circulating eosinophils has been used as a check on the absence of any functioning adrenal tissue remaining in the body. If functioning adrenal tissue is present a significant fall in the circulating eosinophils will occur as shown after unilateral adrenalectomy. A day-to-day record of the excretion of sodium chloride in the urine is kept until a diuresis has been established and a balance between excretion and ingestion can be regulated by administration of the proper amount of sodium chloride to maintain the bodily economy and yet not accumulate an excess of salt and water in the tissues. Herein seems to lie the important physiologic source of any expected improvement from adrenalectomy at the present. Other measurable sources of improvement of a metabolic nature are yet to be demonstrated.

SUMMARY

A preliminary report of bilateral total adrenalectomy for malignant hypertension and chronic nephritis has been made. There were 9 patients in the primarily hypertensive group and five in the nephritic group. Two patients died of renal failure and two of cardiac complications of their vascular disease.

knees, liver enlarged, spleen just palpable Heart grossly enlarged Blood pressure 185/140 Red blood cells 7,400,000 Hemoglobin 19.4 gm per cent

Four hundred cubic centimeters of blood were removed by venesection He was discharged free of edema on July 5, 1947

November 9, 1947, patient re-admitted owing to increasing dyspnea, cyanosis and edema of ankles

The findings were as before but the liver was now palpable 2 inches below costal margin and the spleen palpable with ease The urine contained much protein, an occasional red and white cell, and some granular casts Hemoglobin 136 per cent

On November 12 he complained for the first time of pain in the left side of the abdomen, going down into the testicles, some frequency and dysuria The pain disappeared but the next day he collapsed after using a bed-pan, the heart beat showed irregular changes in rate, and he died on the evening of December 13

Post-mortem examination A well developed young man The body showed striking cyanosis of the face and shoulders, and over the abdomen there was a petechial rash

Skull and contents were not abnormal

The thorax contained small bilateral pleural effusions A very small nodular infarct at each lung apex Respiratory system otherwise appeared natural The pericardium contained an excess of pale yellow fluid The heart was greatly enlarged (750 gm) the right auricle and ventricle preponderating in size Right auricle dilated, foramen ovale closed Tricuspid valve dilated Right ventricle greatly hypertrophied and dilated, its wall 1 cm thick Interventricular septum natural Pulmonary valve natural The pulmonary artery showed atheromatous patches, it was of normal size The ductus arteriosus was patent, its lumen 0.5 cm in diameter Left auricle, mitral valve and left ventricle appeared normal, except for some mottling of the muscle near the apex Left ventricular wall 1.2 cm thick Aortic valve natural Proximal to the ductus arteriosus the aorta showed a mild degree of coarctation, and distal to the ductus the aorta was rather small for the size of the man, elastic, and with minimal signs of atheroma Coronary arteries appeared normal

Apart from the genito-urinary system, the abdominal organs only showed congestive changes, and some submucous and subserous petechiae of the stomach The spleen was very firm and dark (368 gm) Both kidneys were represented by white cystic tumors not covered by perinephric fat (fig 4) The right was the smaller (14 cm long), there were surface irregularities showing variable fluctuation The left was larger (16.5 cm long), its white fibrous wall was firmly adherent to the splenic flexure of the colon, the left suprarenal gland, and the left psoas muscle The kidneys will be further described below Ureter natural The bladder contained a pea-sized submucous nodule projecting in the midline above the trigone The prostate and genitalia were natural The endocrine glands did not appear abnormal There was no lymphadenopathy

Cut surface showed that the right kidney was surrounded by a rind consisting of innumerable cysts containing pale watery fluid here and there of a vel-

DISCUSSION

DR GEORGE F CAHILL (New York, N Y) The work of Dr Thorn and his associates in the investigation of the adrenal has made a number of notable advances in the better understanding of both its normal and abnormal physiology. Based upon reasoning, they offer new experimentation for consideration in certain hypertensives.

The availability of cortisone as well as desoxy corticosterone and of a potent whole adrenal extract has changed the fatal prognosis of an adrenalectomized individual into a life maintenance with a relative normal balance. Dr Thorn and his co-workers have experimentally accepted such maintenance balance as preference to the expected fatal progress in 14 cases of severe malignant hypertension and chronic nephritis. They have discussed their selection of patients within the foregoing described conditions. Their preparation of patients for total adrenalectomy was that which experience has shown to be wise in adrenal surgery where adequate hormonal substitution therapy is necessary. They preferred a one-stage bilateral adrenalectomy if the patient's condition warranted and did only a two-stage operation in the very severe, although from their report the one-stage showed apparently better results in less severe cases. They discussed the operative procedure and preferred a posterolumbar approach for several reasons, all of which are sound because these cases have no explosive hormonal reactions from operative handling and no cellular extension as is possible in carcinoma. The adrenals were presumably normal.

They have described the difficulty in removing normal adrenals because of vascular supply and possibility of gland fragmentation. They suggest also that in bilateral exposure the possibility of a pheochromocytoma or cortical adenoma being present. Because multiple pheochromocytomas are very frequently outside the adrenal and in other ganglia, it has been the opinion of surgeons who have had some experience with these tumors that the diagnoses may be first determined pharmacologically and the tumor removed safest by transverse transperitoneal anterior abdominal incision. Their results apparently justify their procedure of adrenalectomy in the cases reported, even though the operative risk and casualty have been high. Those who recovered have shown a relief of symptoms that made the risk acceptable. This has been similar to the safer prognosis of a myxedema over a toxic thyroid in a somewhat similar situation. Their experience suggests that a greater number of cases should be operated upon to accept its true value even though it appears to offer a substitution of what was once a fatal disease for one which still is often fatal. As yet this is not an established criterion that the adrenals are alone responsible for these hypertensives states.

DR CHARLES B HIGGINS (Chicago, Ill) I think we have listened to one of the great papers of the age.

A few weeks ago I had the great pleasure of visiting a hospital in Boston which among the institutions of medicine in the world, is one of the most exciting

cytes. Cyst not lined by endothelium. Outer cyst wall of almost avascular fibrous tissue, in which were some lymphocytic infiltrations. Capillary engorgement was not a feature on this side.

Iron stains showed iron deposit on the right side in the neighborhood of engorged vessels, but not on the left.

Lung. Arterioles showed medial hypertrophy and some were almost occluded by endarteritis. In one section an infarct was shown.

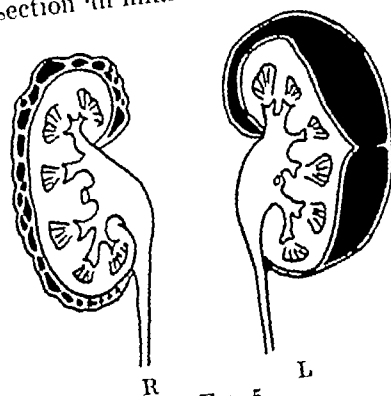


FIG 5



FIG 6 Case 2 Right and left kidney opened to show perinephric cysts (From a color transparency of fresh specimen)

Heart. Some interstitial hemorrhages, but no evidence of infarction.

Liver. Portal infiltration with lymphocytes and early cirrhosis.

Submucous tumor of bladder resembled a "granular myoblastoma." In this case the condition of the kidneys was an accidental finding at post mortem examination. The cause of death was congenital heart disease, a patent ductus arteriosus with pulmonary hypertension and a reversal of flow, so that the right ventricle had to bear the systemic pressure. (This type is discussed by Douglas et al [1947].) During life there had been no history of trauma, and the only sign of renal disease was the occurrence of albuminuria, ascribed to renal congestion.

because of the necessity for greater exposure, particularly in these patients who have greatly enlarged livers. The adrenal can be seen lying distal to the ends of the fingers there. The kidney is under the hand. The liver is seen superiorly.

(Slide) The same exposure at a higher power, with a small Penrose drain around the inferior blood supply of the adrenal going to the renal vessels. It is to be remembered that large vessels coming into the superior pole of the adrenal from the phrenic vessels must be secured initially after dissection, to free the lateral aspect of the gland. Having divided the superior vessels, the gland comes down to you much more easily, and the inferior vessels are then secured.

Here we see the kidney displaced, the adrenal is completely free after the division of the vessels, and is ready for removal.

(Slide) This shows us the size of the average, normal adrenal. Dr. Cahill assumed that these were normal in every patient; these adrenal glands were normal in so far as we have yet determined—normal to ordinary histologic study and normal to special staining techniques. Histochemical studies are being made, and we have not anything to report on those as yet.

I should mention that there has been a discrepancy in size on the two sides. In one instance the adrenal weighed about 6 gm. on one side and 12 gm. on the opposite side.

(Slide) This is to show you the marked contrast of the normal adrenal to that of one of our patients with Cushing's disease or the corticometabolic syndrome of Dr. Cahill. This patient was 50 years old. This gland is not the color of a normal gland. This patient had hypertension, hyperglycemia and glycosuria. We see a gland that is the usual dark brown color of the cortical adenoma of the adrenal. In this instance that is simple hyperplasia, with a marked hyperplasia of the zona glomerulosa.

(Slide) This is another finding in one of the hypertensive patients—a large cystic tumor of the adrenal which was not a pheochromocytoma.

(Slide) This shows us the baseball size of this tumor, which was removed through a posterolateral approach.

I hope that we have not created any misconceptions in the approach to this study, and I wish to emphasize again that this has been a feasible procedure in patients having hypertensive vascular disease who have failed to respond to all of the other forms of therapy. We are looking forward to a further study of the effects of total adrenalectomy upon patients having neoplastic disease, especially carcinoma of the prostate.



FIG 9 Case 2 Right kidney. Section shows dilated venule traversing junction of renal cortex and perinephric tissue ($\times 60$)

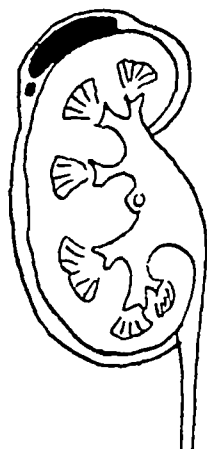


FIG 10

be impossible to say whether a cyst around a hydronephrosis originally contained urine if it is no longer in communication with the pelvis. Some of the cases to be mentioned under other headings may in reality belong to this group.

An important predisposing cause in this condition is urinary obstruction—whether existing before the time of injury, as in rupture of a hydronephrotic kidney (Baretz 1944), or resulting from the injury itself. This is shown by the experimental work of several authors, notably Razzaboni (1922), who produced the condition with some regularity in animals by dividing the pelvi-ureteric junction.

In naturally occurring cases, a blood clot in the pelvis or ureter, or a cicatricial ureteric stenosis, prevents the urine secreted by the kidney from descending by the natural passages, and the raised urinary pressure forces urine through a rent, either in the substance of the kidney or in the pelvis. The capsule may be dissected off the kidney, or urine may escape into the capsula adiposa and produce necrosis and liquefaction of the fat and subsequent encystment. Delbet (1903) stressed infection as an important factor in keeping the wound open.

Occasionally cases are reported in which urinary obstruction is present, but no history of trauma is obtained (Buerger 1914, Zinner 1920). The presence of a fistula between the hydronephrotic and perinephric cavities distinguishes these from the perihydronephrotic cysts of doubtful origin which will be described later. The content of the cyst is seldom chemically analyzed and in any case is likely to give information of equivocal value.

Spontaneous rupture of the kidney has occasionally been due to renal calculi ulcerating through the pelvis. Martineau and Turkel (1948) have recently reported a case and given a bibliography.

PERINEPHRIC HEMATOMA

As a result of trauma to the kidney, e.g. by crushing or in gunshot wounds, bleeding into the perinephric tissues is not uncommon. Spontaneous perinephric hematoma is also a recognized entity, and numerous papers have appeared on the subject. The bleeding may have its source in a ruptured aneurysm, a vessel eroded by carcinoma or tuberculosis or in a variety of other conditions predisposing to bleeding such as periarteritis nodosa and hemorrhagic diatheses. It has been attributed in some cases to arteriosclerosis and older German authors have referred to it as "apoplexy of the renal bed." After these causes have been excluded there remain a number of cases in which no adequate cause has been found.

The characteristic sudden pain and appearance of a tumor in the flank with evidence of exsanguination were described by Wunderlich in his textbook *Handbuch der Pathologie und Therapie* (1856) and have been noted in most cases recorded since. Some earlier mentions of perinephric bleeding are quoted in the historical part of Doll's (1929) exhaustive review of perinephric hematoma.

Polkey and Vinick (1933) have collected 178 cases of nontraumatic perinephric bleeding from the literature, all causes being included. (Some of their cases do not strictly belong in a discussion on perinephric hematoma, being

In support of this would be the dense fibrosis and lymphocytic infiltration. No mention has been made in the earlier part of this paper of infective perinephritis and its sequelae, since there has been no report of cysts resulting from it. By analogy with inflammatory conditions elsewhere, it is not to be expected that a cystic state would arise from inflammation alone, but inflammatory occlusion of the hilar lymphatics is possible, and could be the cause of cysts. The fact that the condition was bilateral makes such an explanation unlikely.

Although some authors have stressed some form of chronic nephritis as an important factor, it is difficult to be sure that the changes found were not secondary. Not only can decapsulation of the kidney by itself cause fibrosis and glomerular atrophy in the cortex (Boncz-Osmolowsky 1903), but fibrosis of the perinephric tissues may cause hypertension and eventually the renal changes that result from it (Page 1939). Even if degenerative changes were found in the kidney in all cases, it would still be unjustifiable to consider them an important cause of such a rare condition.

The changes found in cases 2 and 3 are therefore best interpreted as sequels of perinephric bleeding.

The origin of the perihydronephrotic cyst is even more obscure. The occurrence of urinary cysts around hydronephrotic kidneys, even without a discoverable fistula connecting the two cavities, and the variable presence of blood or clots in the sac, make the cases difficult to classify.

Ureteral ligation in the dog (Winternitz and Katzenstein 1940) has been found to result in perinephric collections of friable red material, as well as lymphatic and venous distension. Little et al (1947) have also produced frank perinephric hemorrhage in dogs by ureteral ligation and dosage with phthalyl-sulfathiazole, ligation alone did not produce hemorrhage.

After describing a case of perinephric cyst around a hydronephrotic kidney, Schopper (1937) notes that India ink, injected into the tied-off ureter of a rabbit, rapidly enters the venous system by the pyelovenous reflux and reaches as far as the fibrous capsule. He did not demonstrate any striking accumulation of ink beneath the capsule, nor has this been observed by others in experiments of this sort. In the discussion which follows, Gruber suggests a pyelo-interstitial or pyelo-lymphatic reflux as a more likely cause of the perihydronephrotic cysts. This hypothesis certainly would explain the rarity of the condition, for as Abeshouse (1934) points out, pyelolymphatic reflux is demonstrated so rarely in retrograde pyelograms that some anatomical anomaly must be the cause. There has been some skepticism about lymphatic filling as the true explanation of the pyelographic appearances described as "pyelolymphatic reflux," but at all events opaque material appears to reach the perinephric tissues without evidence of trauma from the catheter, and to remain longer than would be possible if it lay in the veins (de la Peña 1944).

The conception of a urinary reflux is supported by a case (Coenen and Silberberg 1923, Coenen 1923) in which ingested methylene blue could be demonstrated in a perihydronephrotic cyst not communicating with the pelvis. It will be time to reconsider the question when the mechanics of hydronephrosis and of the reflux phenomena are better understood.

A case which probably belongs here is that of Shih and Wu (1941), a woman of 38 with 3 months' history of pain in the right flank. A loculated cyst covered the lateral aspect of the right kidney, its wall was of dense fibrous tissue, continuous with the fibrous capsule of the kidney, and it contained dark fluid and fibrin. The photograph shows that the kidney was slightly compressed by the cyst, and did not lie free within it. The authors are in doubt whether to postulate a hemorrhagic or a lymphatic origin. Lippens (1911) described a case showing

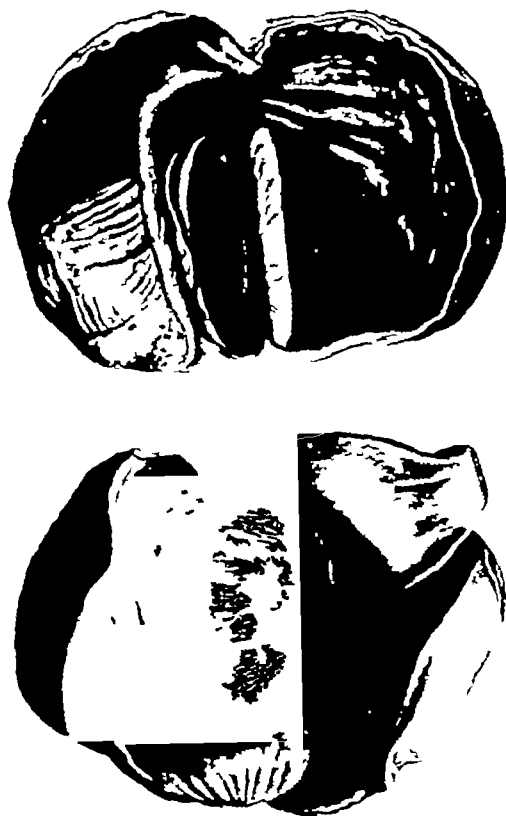


FIG. 1. Bilateral spontaneous perinephric hematoma. Case of Koch, 1909. Reproduced from Coehen, H. (*Beitr. z. klin. Chir.*, 70: 494, 1910.)

much greater distortion of the kidney, but otherwise similar. The history resembled that of perinephric hematoma.

Miller and Cordonnier (1949) have reported another similar case in this journal. Removal of the affected kidney rapidly relieved severe hypertension.

Etiology. The cause of "spontaneous" perinephric hematoma has been much disputed. In the *Deutsche Zeitschrift für Chirurgie* of 1912 alternate papers can be found from Ricker, supporting his theory of diapedesis in stasis from vasomotor exhaustion (Ricker 1911) and from Löwen, who maintained that massive bleeding occurs in eroded or ruptured vessel. Fahr (1926) following Coenen,

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The case of Hoffmann (1896) is in some ways similar, only the description of the specimen is available. There was carcinomatous infiltration of the hilum of the kidney. A cyst about the size of a fist partially surrounded the kidney, in the rest of the fibrous capsule numerous cysts of all sizes up to that of a hazelnut. The smallest cysts, representing tissue spaces, had no endothelial lining,

TABLE 1

AUTHOR	CAUSES OF OBSTRUCTION	FLUID	REMARKS
Albarran 1899	>	Hemorrhagic	Subcapsular Few details given
Azzurrini 1912	Carcinoma uterus	Sero-hemorrhagic	Thick-walled cyst lined by clot
Löwenstein 1920	>	Slightly cloudy, yellow	Extracapsular, thick-walled
Sohn 1921 (2nd case)	Carcinoma cervix uteri	Reddish-yellow	Intracapsular Foci of hemorrhage in wall
Krogus 1921 (1st case)	Carcinoma uterus	Clear, brownish	Subcapsular Very large cyst
Minet 1921	>	Brown	Interstitial nephritis Old history of trauma, possible urinary origin
Johnstone and Browne 1921	Congen ureteric stenosis	Slightly blood-stained	Newborn Subcapsular
Connerth 1922 (1st case)	Mxoblastic sarcoma of bladder	Clear, pale yellow	Bilateral, infant 20 months Walls lined by clot Subcapsular
Coenen and Silberberg 1923	Carcinoma bladder	Clear, pale yellow	Bilateral, intracapsular
Slobotziano et al 1929	>	Clear	Newborn notencephalic monster, other kidney polycystic
Rizzi 1936	Carcinoma cervix uteri	Turbid, hemorrhagic	Subcapsular, walls showed old and recent hemorrhage
Schopper 1937	Urethral valve	Clear, alb +	Bilateral, infant 17 days Intracapsular Chronic interstitial nephritis
Müller 1926	Carcinoma rectum	Clear	Laver of multiple cysts

but the main cyst which was trabeculated, was mostly lined by a single endothelial layer. The fluid was rich in albumin.

It is probably justifiable to conclude, from this series of obstructive cases, that obstruction of lymphatics at the hilum of the kidney can be additional, if not a sole cause of perinephric subcapsular or intracapsular effusions, and that these are not necessarily the result of hemorrhage.

Although the fully developed picture, as in the cases included in table 1, is

attacks those who claim a high incidence of surgical renal disease in hypertensive patients. He shows that their statistics are incorrect and concludes that unilateral renal disease is rarely a cause of hypertension in man, that the theory of primary renal origin of hypertension is unproved and that the kidney appears to be the victim rather than the culprit.

MATERIAL

The 92 hypertensive patients studied are among the 316 consecutive nephrectomies at Duke University Hospital. For comparative information 65,479 consecutive admissions to this hospital from 1940 through 1944 are reviewed to determine the incidence of hypertension and of surgical renal disease in hospitalized patients.

CRITERIA OF HYPERTENSION

A systolic blood pressure of 140 mm Hg and/or a diastolic pressure of 90 mm Hg are chosen as the low limits of hypertension. This seems reasonable since these points are generally accepted as beginning hypertension.⁷

INCIDENCE OF HYPERTENSION

Among the 316 nephrectomy patients 92 or 29.1 per cent had essential hypertension. This contrasts with 7,574 or 11.5 per cent patients with essential hypertension in the 65,479 consecutive hospital admissions. It is apparent that the incidence of hypertension in the nephrectomy group, representing advanced surgical renal disease, is approximately three times greater than in general hospital admissions. This fact supports the theory that surgical renal disease may be the initiating factor in the pathogenesis of certain hypertension.

There were 1,183 patients with all types of surgical renal disease among the consecutive admissions. Of these 163 or 13.7 per cent had hypertension. This is a much lower incidence than in the reported nephrectomy group. It may be due, in part, to the fact that all types of surgical renal lesions are included and therefore many of them not as far advanced as those in the nephrectomy group.

The incidence of hypertension was determined in each type of surgical renal lesion encountered (table 1). It was found highest in those patients with renal tumors. Here one must consider the important role played by age. Sixty-one per cent of tumor patients were over 50 years of age. It is interesting to note that none of the 3 patients with chronic pyelonephritis without atrophy had hypertension.

Many observers have noted the high incidence of hypertension in the presence of obstruction in the urinary tract. All urologists have observed the frequency of hypertension in patients with bladder neck obstruction. The prompt decrease in blood pressure in many patients following relief of the obstruction is familiar to all of us. The rate of occurrence of hypertension in patients with hydronephrosis is not as high as in certain other renal diseases. However, the postoperative rate of return to normal blood pressure, as will be seen later, is highest in such patients. One of the patients in this study illustrates this point very nicely. He

⁷ Robinson, S. C. and Brucer, M. Range of normal blood pressure. A statistical and clinical study of 11,383 persons. Arch. Int. Med., 64: 409-444, 1939.

Examples of paranephric cysts are the hilar lymphatic cysts, which are usually very small and may be multiple and bilateral (Henthorne 1938, Scholl 1948), and solitary cysts lined by epithelium, lying beside and sometimes compressing the kidney, and sometimes communicating with the pelvis. Origin from the wolffian body has been postulated for some of these. Retroperitoneal lymphangiomas, if extending at all laterally, can hardly fail to involve the region of the kidneys. It is not proposed to review the subject of retroperitoneal cysts in this paper.

Perinephric cysts containing clear fluid occur in domestic animals, especially in the pig. Schmev (1915) and Joest (1923) give descriptions of these; they are very large, thin walled, and may be bilateral, they surround the kidneys entirely being attached at the hilum and contain clear yellow fluid. Schmev found that

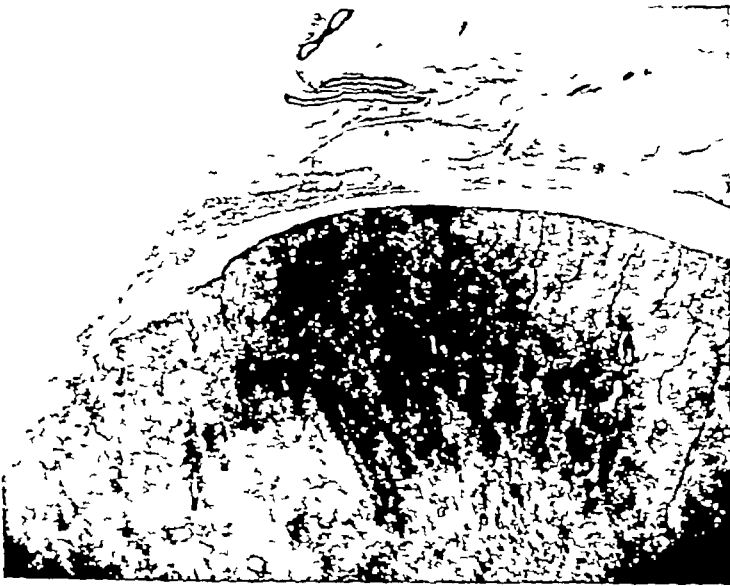


FIG. 3. Case 1. Section from upper pole of left kidney. Subcapsular effusion of fluid with marked capsular thickening ($\times 4$).

the fluid was extracapsular, Joest, on the other hand, was at pains to prove that the fibrous capsule divided to enclose the fluid between its layers. (This appearance is described by Schopper [1937] from an obstructive human case already referred to in table 1.) In assessing the value of studies which attempt to prove the location of the fluid relative to the fibrous capsule, it is important to remember the speed with which connective tissue forms and adapts itself to lines of stress.

It has been repeatedly shown since the earliest years of this century (Albarran and Bernard 1902) that a desecapsulated kidney forms a new and thicker capsule over its surface in a few weeks, hence the examination of the point of reflexion of a cyst wall will almost certainly show two diverging layers, wherever the fluid originally formed.

Malherbe (1890) described a very large perinephric cyst in a man of 28 with a long history of renal colic. Repeated puncture produced several litres of sero-

of these cases The greater percentage of all renal surgery is done in the presence of a urinary tract infection

INCIDENCE OF SURGICAL RENAL DISEASE

Among the 65,479 consecutive admissions reported above, there were 1,183 (1.8 per cent) patients with surgical renal diseases of all types Of the 7,574 hypertensive patients found in this large group of admissions there were 163 (2.2 per cent) patients with all types of surgical renal diseases It appears that the incidence of surgical renal disease in a group of consecutive admissions and a group of hypertensive patients is about the same This indicates that surgical renal diseases appear to be only a small, possible contributor to the genesis of hypertension This agrees with Homer Smith's contention that this incidence is low The high incidence of hypertension among patients with advanced surgical renal disease is of more significance It lends support to the theory that such disease is an etiologic factor in some cases of hypertension

CLASSIFICATION

For this study all hypertensive patients are classified into three groups Class 1, or mild group, includes those with a systolic blood pressure of 140 to 159 mm Hg inclusive and/or a diastolic pressure of 90 to 99 mm Hg inclusive Class 2, or the moderate group, includes those with a systolic blood pressure of 160 to 199 mm Hg and/or a diastolic of 100 to 109 mm Hg inclusive Class 3, or the severe group, includes those with a systolic blood pressure of 200 or more mm Hg and/or a diastolic of 110 or more mm Hg Among the 92 hypertensive nephrectomies there were 32 (34.7 per cent) patients in class 1, 31 (33.8 per cent) in class 2, and 29 (31.5 per cent) in class 3 It is evident that there is an even distribution of patients throughout the three classes

In comparing age and degree of hypertension one finds that the highest per cent of patients in the 0-30 years age group is in the mild class, in the 31-50 years age group in the severe class and in those over 50 years of age in the moderate class It appears that the middle age group tends to develop the severe type of hypertension more frequently than others

The length of the history of urinary tract disease appears to have no significant correlation with the severity of the hypertension, but it must be realized that the duration of the disease cannot be accurately determined by the length of urinary tract symptoms

SEX

The female contributes a slightly higher per cent of patients to the hypertensive and surgical renal disease groups than does the male Sex appears to play no significant role in the incidence of either disease

AGE

A study of the age distribution is interesting and throws some light on the incidence of hypertension in the group The average age of the 316 nephrectomies is 38 years, of the 92 hypertensive nephrectomies 44 years, and of the 224 nor-

containing pale yellowish or watery fluid. In the blood-containing cavity, no visceral layer was to be seen, while the parietal was thick and contained interstitial hemorrhages. The smaller cysts showed visceral and parietal layers, with adherent coagula. One, containing clear fluid, showed no remains of hemorrhage, the lining being hard and white.

Much the same picture was seen in the right kidney. A large cystic space with brownish-red contents surrounded the whole hilum, and beside it on anterior surface and convexity were other little cysts with yellowish or clear contents. Kidney surface bluish red with petechiae. Pelvis not dilated. Other features were those of congestive cardiac failure and cyanosis, and pachymeningitis hemorrhagica interna.

Histology. Extreme vascular congestion of kidneys, especially near surface, and interstitial hemorrhages.

Where present the capsule was very congested and showed hemorrhages. Where fresh bleeding had occurred the capsule was absent, i.e. was separated off the kidney. Cysts containing clear fluid had both visceral and parietal fibrous walls.

Cyst walls showed some hemorrhages and lymphocytic collections, and phagocytosed iron pigment, but this was scanty in the walls of the cysts containing clear fluid.

The author considers the condition a sequel of subcapsular perinephric hematoma, and an early stage of "perirenal hygroma", conditioned by the extreme congestion of the kidneys.

The following case of congenital heart disease with polycythemia and perinephric cysts was recently seen here, and formed the basis for this review.

(*Case 2*) Post-mortem 541/1947. A. T., aged 26, a bricklayer. No relevant family history. All his life he had easily got out of breath on exertion, and was thought to have a weak heart. No history of trauma.

In 1946 he was in bed for 7 weeks with breathlessness and swelling of ankles, during this time he had two hemoptyses.

Admitted to the Radcliffe Infirmary January 27, 1947 (Hosp. Reg. No. 6777/47) because of dyspnea preventing him from working, and a few days' jaundice and dark urine. He was found to have infective hepatitis, and made a normal recovery from this. In addition, he was found to be slightly cyanosed, to have an enlarged heart, a palpable systolic thrill, a loud systolic murmur, loudest in third left interspace, and a reduplicated pulmonary second sound.

Nothing abnormal was palpated in the abdomen. The urine contained albumin. Blood urea 26 mg. per cent, and urea clearance 91 per cent of normal. Red blood cells 6,670,000. Hemoglobin 128 per cent. X-ray and barium swallow showed 1) heart enlarged to right and left, 2) enlarged right auricle, 3) large pulmonary artery, 4) small aorta. An electrocardiogram showed right axis deviation.

It was thought that the cardiac lesion was congenital, and that the albuminuria was due to polycythemia and congestion of the kidneys.

June 16, 1947, patient re-admitted in congestive cardiac failure, edema up to

favorable results then a total of 36 or 53.7 per cent of the patients are benefited. Since hypertension can run a benign course for many years, showing fluctuations in the height of pressure over this time, it cannot be assumed that these patients, who are apparently improved, show favorable results. Therefore, we will consider only those patients with normotension two or more years after operation as favorable results.

The apparent duration of the renal disease, by history, has no significant effect on the post-nephrectomy results. As mentioned earlier, history is not always a good indicator of the duration of the disease. Many patients with severe surgical renal disease remain asymptomatic for long periods.

Some investigators believe that if the hypertension is due to a renal lesion, rest and sedation should not alter it in any way. All patients were studied with a view of determining whether the effect of preoperative bed rest upon the blood pressure had any significant bearing on the outcome of the disease. There was no significant difference in the postoperative course of those who showed im-

TABLE 3 *Postoperative results in each preoperative class of hypertension*

PRE-OP CLASS	TOTAL PATIENTS WITH KNOWN RESULTS	NORMAL BLOOD PRESSURE	
		Patients	Per cent
I-Mild	26	15	58
II-Moderate	21	5	24
III-Severe	20	3	15
Total	67	23	34.3

provement and of those who showed no improvement with bed rest preoperatively.

Patients with and without evidence of cardiovascular disease were studied to determine if the presence or absence of such disease was a good indicator of the outcome. The percentage of patients coming to normal among those without evidence of cardiovascular disease is about two times greater than among those with cardiovascular disease. This fact may be helpful in making a decision regarding operation in certain equivocal cases.

A study of the postoperative results in each of the three preoperative classifications (table 3) reveals that best results are obtained in the mild hypertensive patients, 58 per cent of whom came to normal. As the severity of the hypertension increases, the post-nephrectomy results become less satisfactory. The average age of those patients who came to normal was 34 years, 12 years younger than those who remained elevated. It appears that it is the young patient with mild hypertension who benefits most from nephrectomy.

SUMMARY

The incidence of hypertension in a group of patients subjected to nephrectomy because of advanced surgical disease of the kidney is significantly higher (29 per cent) than in a group of consecutive hospital admissions (11.5 per cent).

lowish tinge. Total length 14 cm, total breadth 8 cm. The kidney was not distorted, but showed congestion and streaky pallor. Length 11.5 cm, breadth 7 cm, anteroposterior 5 cm. The cyst walls were up to 1 mm thick, but mostly much thinner (See figures 5 and 6).

The left kidney was enclosed in a loculated cystic cavity, divided into an upper and several lower compartments. The posterior surface of the kidney was entirely free in the cavity, and the lower pole was also free. On the anterior aspect the cyst extended over less than half the breadth of the kidney, so that the upper medial area next the pelvis was covered by thickened capsule only. The fluid was like clear urine. Total length 16.5 cm, breadth 11 cm, anteroposterior 7 cm. Cyst wall 2-3 mm thick. The kidney was slightly distorted by the loculations of the sac, but its parenchyma was of normal thickness. Its appearance was

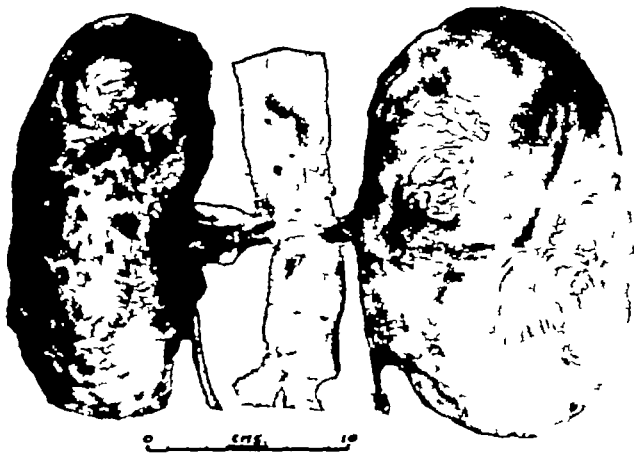


FIG. 4. Case 2. General view of kidneys before section.

pale and streaky. It was covered by a fibrous capsule of about normal thickness but white in color. Length of kidney 15 cm, breadth 5-7 cm.

Histological examination. All the organs showed marked congestion.

The right renal cortex showed very severe congestion with large cellular glomeruli. Tubules showed cloudy swelling and autolytic changes. Arterioles showed sclerosis with partial occlusion. Superficially, some edema and lymphocytic infiltration. In place of fibrous capsule there was a wide zone of fine connective tissue with dilated lymph spaces, engorged capillaries and numerous small interstitial hemorrhages. Dilated venules ran between the renal cortex and the cystic zone. Further peripherally were larger cystic spaces, some showing a partial flattened endothelial lining. The extreme periphery consisted of fibrous tissue and a little fat with intense engorgement, interstitial hemorrhages, and collections of lymphocytes (See figures 7, 8 and 9).

The cortex of the left kidney showed similar changes to the right but with much less engorgement. The glomeruli were strikingly cellular. The cortex was covered by a capsule of dense fibrous tissue containing collections of lympho-

Hans Selye's excellent work⁹ on "The General-Adaptation Syndrome and the Diseases of Adaptation" may eventually lead to the answer in this search for the etiology of essential hypertension. It is conceivable that a surgical renal disease may act as his so-called "stress factor," as might any disease process in the body, and thus lead to hypertension as one of the adaptation reactions.

CONCLUSION

Only 2 per cent of all essential hypertensive patients will be found to have a surgical renal disease. Consequently it is felt that a complete urologic survey, to include excretory urography and, if necessary, retrograde pyelography is not warranted in all patients with essential hypertension. The complete examination should be made only if the preliminary history, physical examination, laboratory findings, and plain x-ray of the abdomen indicate the necessity for further study.

In a carefully selected group of patients with essential hypertension in association with unilateral surgical renal disease, one can expect about 34 per cent to return to permanent normotension following nephrectomy.

In closing, it is well to reiterate what others have stated, namely, that nephrectomy should be employed in hypertensive patients only when there exists a recognized surgical indication.

We wish to express our appreciation to Dr Brodie C Nalle, Jr, Lovelace Clinic, Albuquerque, New Mexico for his assistance in initiating this study.
*Division of Urology, Ohio State University and Medical School, Columbus, Ohio (A.D.P.),
Duke Hospital, Durham, N C (E P A)*

⁹ Selye, H. *Textbook of Endocrinology*. Atca Endocrinologica Université De Montreal, Montreal, Canada.

A milder example of what may be the same process is seen in the following case, kindly communicated to me by Dr C V Harrison

Case 3 Female aged 17 Since age 6 known to have heart disease Admitted to Hammersmith L C C Hospital in November 1947 for uterine hemorrhage



FIG 7 Case 2 Surface of right kidney showing vascular engorgement and cystic transformation of capsule (X8)



FIG 8 Case 2 Surface of right kidney showing perinephric cysts (X4)

Found to be cyanosed, with clubbing of fingers Red blood cells 7 600,000 Hemoglobin 140 per cent Findings were those of Fallot's tetralogy On March 30, 1948 in exploration was done but Blalock's operation was found not to be feasible Died April 1, 1948

Post Mortem 4320 Fallot's tetralogy confirmed Right hemothorax Caseous tuberculous ileocecal glands and tuberculosis left ovary and both fallopian tubes

benefit of such operations. In the charity hospital total admissions have not markedly increased (254,752 to 302,240), while nephrectomies have increased more than three fold (86 to 293). In this institution admissions have been limited by lack of beds, so that only the most severely ill are admitted to most services. This applies to urologic patients and to a large part accounts for the lack of correlation noted in the private institutions.

Analysis of renal diseases requiring nephrectomy has previously revealed that the operation has been more commonly performed in female than in male patients. A review of figure 2, A shows that this tendency remains. It would appear that there is a greater proportion of females to males in the charity patients than there is in the private patients. As to the reasons for this, it was found that the charity case has received less effective preventive urological

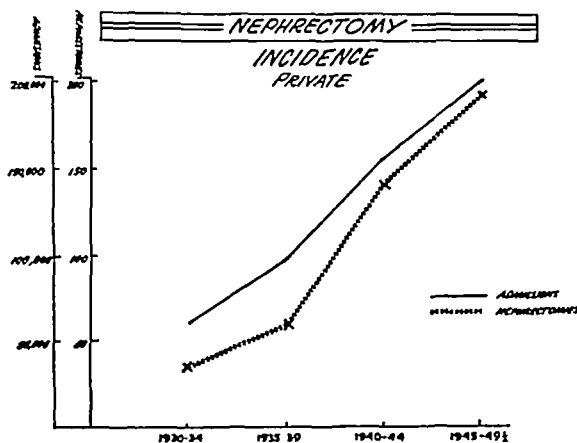


Fig 1

treatment, particularly for infection, to which the female is more vulnerable than the male.

When these patients were analyzed as to age, it was found that both in the charity and in the private patients an older age is being attained before nephrectomy is required (fig 2, B). When one studies figure 2 it is noted that there is a relative decrease in those patients between the ages of 10 and 19 who have required nephrectomy. Cases in this particular age are made up principally of those in whom the etiology is infection or trauma. The patients from birth to nine years are principally those with Wilms' tumors and congenital hydronephrosis. It is notable that there has been a marked increase in the number of such patients. The fact that malignancies have been more frequently recognized has some influence on the change in the overall age picture. Among patients 70 or over, it is notable that the operation has been somewhat extended due to our better understanding of disorders of the aged and their ability to withstand major surgical procedures.

THE DIAGNOSES

As one would anticipate, the principal disease processes necessitating nephrectomy were infection and hydronephrosis with or without calculus forma-

Fibrous capsule of right kidney was a little thickened, and this thickening spread to a slight extent into the adjacent fat. The kidney itself appeared normal. Fibrous capsule of left kidney greatly thickened (about 1 mm), and this fibrosis spread into the adjacent fat as if there has been perinephritis. Near the upper pole of the kidney anteriorly, there was a flat clear cyst, about 7 by 3 by 1 cm, containing watery fluid (fig 10). The underlying kidney appeared healthy. On both sides the fibrous capsules stripped easily leaving a smooth kidney. Ureters and bladder normal.

Histology. Fibrous capsule of right kidney thicker than normal, and showing capillary congestion and some extravasated red cells. Cortex very congested. Glomeruli swollen, cellular and in many cases extremely congested with blood. Some are sclerotic. Tubules show varying stages of degeneration.

Fibrous capsule of left kidney greatly thickened, with numerous dilated lymphatics and tissue spaces. It does not show capillary congestion. Renal cortex shows the same changes as the right kidney, but congestion is not so extreme. Arterioles show thickening and irregularity of all coats. Sections stained for iron show no deposits.

DISCUSSION

Cases 2 and 3 may probably be regarded as different degrees of the same process.

In the absence of trauma or of hydronephrosis we may be satisfied that the condition was not due to extravasation of urine. Possible causes are 1) organized spontaneous perinephric hematoma, 2) lymphangiectasis, congenital or obstructive, and 3) resolved perinephritis.

The hematoma theory has its support in the histological findings on the right side in case 2, the comparative frequency of perinephric bleeding, and the presence of a probable etiological factor (polycythemia). As we have seen, polycythemia has been noted in frank perinephric hematoma (MacKenzie 1930), in encysted and organized hematoma in a case strikingly similar to these (Löfner 1927), and in two perfectly organized serous cysts which are most probably a late result of the same process (Minkowski 1906, Rennen 1923).

In favor of the lymphangiectasis theory, it must be admitted that lymph spaces with endothelial linings were present on the right side, in case 2, and appeared to form cysts. Also, the fluid, however it originated, had been replaced by lymph. Probably venous and lymphatic engorgement have combined to produce the final picture. In lymphatic obstruction due to filariasis, chyluria may occur, and retroperitoneal lymphangioma is described, but nothing resembling perinephric cysts.

As a congenital or neoplastic condition, lymphangioma in this area is known, but does not resemble this, it involves the retroperitoneal tissues without confining itself to the limits of the perinephric fat.

The association of the perinephric cysts with other congenital anomalies certainly deserves notice, but these defects were in all cases the cause of polycythemia and therefore of renal congestion.

Finally, the possibility remains that this condition results from inflammation

more careful and if necessary prolonged investigation is warranted. Diseased ectopic kidneys comprised 9 cases. There were 7 cases of horseshoe kidneys and 4 congenitally polycystic kidneys. There were 5 sarcomas (the Wilms' tumors were included under the carcinomas) and 2 adenomas of the kidney. Two nephrectomies were performed because of extension of adrenal carcinoma into the kidney. There were 2 cases in which ectopic ureters had vaginal orifices and heminephrectomies were performed. Two instances of marked varicosities of the renal pelvis led to difficulty necessitating nephrectomy. There were 3 primary carcinomas of the ureter, 1 hypoplastic kidney, 1 unclassified urogenital ridge tumor, 1 hemangioma of the ureter, 1 aneurysm of the renal artery, 1 fibroleiomyoma, an instance of unexplained subcapsular hematoma, 1 perirenal hematoma, 1 case with hydro-ureter with renal metastatic carcinoma originating in the cervix uteri, 1 instance of a large pancreatic cyst with associated renal destruction, 1 hematoma of the kidney in the newborn, 1 case of hydro-

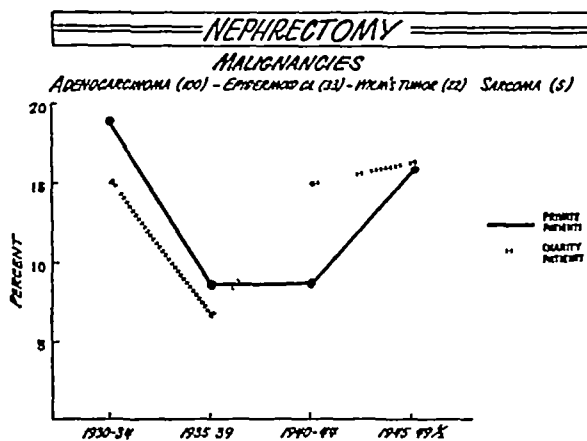


FIG 3

cephalus in which a normal kidney was removed in order to utilize the ureter for subarachnoid anastomosis for hydrocephalus.

MALIGNANCIES

When one studies the various malignancies it was found that 100 were adenocarcinoma, 33 were epidermoid in character, there were 22 Wilms' tumors and 5 sarcomas. There has been a progressive increase in the number of malignancies removed. In figure 3 it was noticeable that the highest percentage was during the first period under consideration, when there was the smallest total number of nephrectomies. This occurred not because of ability to diagnose neoplasm then but because of smallness of the total number of nephrectomies and due to failure of application of proper diagnostic methods in recognition of other diseases requiring nephrectomy. This graph tends to indicate that we are beginning to definitely increase the number of patients given benefit of nephrectomy for malignancy of the kidney. However, study of mortality of these patients reveals that in most instances the diagnosis is entirely too late.

SUMMARY

The literature of perinephric cysts is reviewed, and the origin of some of them from hematomas and effusion of urine around the kidney is discussed. Special interest attaches to those of unknown origin, of which very few have been reported, the majority have been associated with hydronephrosis. An early case of this type is described.

Two cases are reported of secondary polycythemia with abnormal appearances of the renal fibrous capsules. One is a well-developed example of bilateral perinephric cyst formation in a young man dying of congenital heart disease. These cysts are interpreted as sequels of perinephric bleeding.

ADDENDUM

Since going to press, the following remarkable case occurred here, and is briefly reported with grateful acknowledgement to Mr. Elliot Smith, and to Dr. P. C. Elms who performed the post-mortem examination.

R. F., P. M. No. 114/1950. Male aged 38. Six months' history of right loin pain, intermittent hematuria, anorexia and vomiting. Palpable left kidney. Died in uremia with a provisional diagnosis of polycystic kidneys.

At post-mortem examination the right kidney was found to be pyonephrotic with no remaining renal tissue. The left ureter was obstructed by a small carcinoma of the bladder involving the ureteral orifice. The right kidney was represented by a tumor weighing 2000 gm., consisting of the enlarged kidney with dilated calyces and pelvis, and surrounded by an organizing perinephric hematoma. The cavity of the cyst enveloping the kidney contained about 600 cc. of clear fluid, as well as partially organized clot on the kidney surface. Microscopically, the renal capsule appeared much thickened, and the surface of the kidney showed dense fibrous tissue below the layers of organizing clot, the appearance was produced of the capsule being divided into two layers to enclose the cyst. The parenchyma of the kidney was not particularly congested, but showed evidence of pyelonephritis.

This case may be classified with the obstructive cases in table 1 which show unequivocal evidence of subcapsular bleeding.

I am indebted to Professor L. J. Witts for permission to publish case 2, and to Dr. C. V. Harrison and Professor J. McMichael for access to and permission to publish case 3.

I am also very grateful to Dr. G. A. C. Summers for the photographs, and to Dr. A. H. T. Robb-Smith for all his advice and help in the preparation of the paper.

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in the private and the charity cases there has been a decline (Private cases from 8.2 to 2.7 per cent, charity cases from 10.3 to 4.7 per cent.) Study of the overall mortality from nephrectomy reveals the highest mortality occurred in the cases of nonsurgical trauma (19 per cent). During the last period this percentage has decreased to 10 per cent. It is evident that there will continue to be a high mortality among these patients for many have marked associated injury to the spleen, gastro-intestinal tract, liver, diaphragm, chest, brain or other important organs.

Of the patients with cancer, the total hospital mortality was 11.5 per cent. During the last period under consideration, only 3 per cent of these private patients and 7.7 per cent of the charity cases expired while in the hospital.

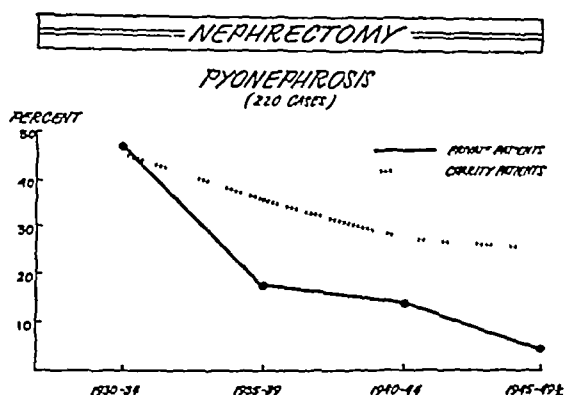


FIG 4

TABLE 1 *Nephrectomy*

Calculi associated with hydronephrosis, pyonephrosis and pyelonephritis (484 of 806 patients)

	1930-34	1935-39	1940-44	1945-49½
Private	60%	41%	59%	41%
Charity	61%	51%	62%	66%

Perhaps the principal reason for this difference is the better education of private patients, which leads them to seek proper diagnosis earlier.

For the entire group of patients with pyonephrosis the hospital mortality was 8.6 per cent, while during the 1945-49½ period only 3.6 per cent of such patients expired. There has been a marked decrease in the percentage of patients requiring nephrectomy because of uncontrolled cortical infection with abscess formation. The mortality in this group remains high. During the last 5 years 14 per cent of these patients expired. This high death rate can be explained by the fact that these patients represent those for whom the available antibacterial agents have been employed without success and as a last resort nephrectomy is performed. It is little wonder that with bacterial resistance to the available agents they succumb to spread of infection. As well, among this group were found those with increased susceptibility to infection due to conditions such as diabetes mellitus.

HYPERTENSION AND THE SURGICAL KIDNEY

ALLEN D. PUPPEL AND EDWIN P. ALYEA

*From the Department of Surgery, Division of Urology, Duke University Hospital
and Medical School, Durham, N. C.*

It is our purpose to report the results of a detailed study of a group of patients with essential hypertension in association with unilateral surgical renal disease and upon whom a nephrectomy was performed. Among other things it is hoped that such a review will answer the question of whether or not it is absolutely necessary to make a detailed urologic study of each patient with essential hypertension. Of course, we are also interested in knowing the percentage of patients who are cured of hypertension by removal of the diseased kidney.

The close association of hypertension and renal disease has been recognized since Bright's¹ observations on this subject more than a hundred years ago. In 1898 Tiegerstedt and Bergmann² reported their demonstration of the presence of a pressor substance, which they called "renin", in the saline extract of a normal rabbit kidney. This work has been confirmed. It has been shown that it is present in greater concentration in the extract of the ischemic kidney.

The exact site of production of renin in the kidney is debatable. At present it is thought that it is produced by the proximal convoluted tubules.³

Page⁴ has shown that renin by itself is not a pressor agent but requires activation by hypertensinogen (angiotonin precursor). It is thought that this substance is produced by the liver. The resulting substance is hypertensin (angiotonin), the pressor agent. Hypertensin is destroyed by an enzyme, hypertensinase, which is produced by normal renal tissue. Therefore, hypertension can result from an overproduction of hypertensin or a lack of hypertensinase.

Goldblatt and coworkers⁵ provided the stimulus which has created increased interest in this subject during the past two decades. Their conclusion was, that in dogs at least, ischemia localized to the kidneys is a sufficient condition for the production of persistent hypertension of a type that resembles that which is associated with arteriolar nephrosclerosis in man.

Reports of clinical observations and investigations on this subject during the past two decades have been numerous. A review of these reports is not included herein.

Homer Smith⁶ in discussing the role of the kidney in the genesis of hypertension

Read at annual meeting, Southeastern Section, American Urological Association, Memphis, Tenn., March 8, 1951.

¹ Bright, R. Cases and observations illustrative of renal disease accompanied with the secretion of albuminous urine. *Guy's Hospital Report*, 1: 338, 1836.

² Tiegerstedt, R. and Bergmann, P. G. Niere und Kreislauf Skandinav. Arch. f. Physiol., 6: 223, 1898.

³ Oliver, J. When is the kidney not a kidney? *J. Urol.*, 63: 373, 1950.

⁴ Page, I. H. On the nature of the pressor action of renin. *J. Exp. Med.*, 70: 521, 1939.

⁵ Goldblatt, H. Studies on experimental hypertension. XII. The experimental production and pathogenesis of hypertension due to renal ischemia. *Am. J. Clin. Path.*, 10: 40-72, 1950.

⁶ Smith, H. W., Goldring, Wm. and Chasis, H. Role of the kidney in the genesis of hypertension. *Bull. N. Y. Acad. Med.*, 19: 449, 1943.

employed Prior to 1945, ninety-three or more per cent of patients did not receive any blood either pre- or postoperatively Since 1945, 49 per cent of the cases received one transfusion Eleven per cent received 1000 cc of blood and 3 per cent received over 1000 cc This latter group is composed principally of patients experiencing marked hemorrhage at the time of operation The utilization of blood transfusions preoperatively to restore the peripheral blood picture to a safe level and replacement of blood loss at operation in excess of 300 or 400 cc are becoming generally adopted procedures Most surgeons wisely provide matched blood or suitable donors in their preoperative preparation of the patient

ANESTHESIA

During the last 20 years spinal anesthesia has become more popular and cyclopropane came into common usage after 1940, therefore it is natural that there would be some change in the utilization of these particular agents as compared with the previously more frequently used ethylene and ethyl ether At the charity institution in the earlier years the urologists had grown to like spinal anesthesia particularly since they had found it successful when applied as "a saddle block" in transurethral resections or in suprapubic cystotomies for patients who did not tolerate surgery well However, the advent of a school of anesthesia in this charity institution has had considerable influence in decreasing the frequency of administration of spinal anesthesia for nephrectomy The need of patients to teach nurse anesthetists to use the general anesthetic gases has led to some increase in the frequency of utilization of ethylene, ether, and cyclopropane In the private institutions there has been a definite increase in the number of patients in whom spinal anesthesia has been administered In this entire group of cases, from the study of the records, it was not definite that any death was directly due to the anesthesia but it is possible that in some of those experiencing shock at the time of operation in the absence of marked blood loss the anesthetic may have played an important role Certainly selection of the anesthetic agent is a matter of individualization of patients

POSTOPERATIVE STAY OF PATIENTS

More patients are being discharged from the hospital in less than 15 days This trend is more marked for the private patients (24.3 per cent, 42.6 per cent, 59.9 per cent and 68.4 per cent as compared with 16.3 per cent, 17.3 per cent, 21 per cent and 42.7 per cent) and is to be correlated with the fact that their lesser degree of pathologic renal involvement and nonurinary disorder as compared with the charity cases The earlier discharge from the hospital indicates improved preoperative care as well as improved postoperative care with early ambulation

CONCLUSIONS

From January 1, 1930 to July 1, 1950 there has been a progressive increase in the number of nephrectomies performed at two private general hospitals and one large charity hospital in New Orleans This increase is related to increased hospitalization and to increased diagnostic investigation of patients

is a 51 year old white man who was first seen at Duke Hospital in January 1938, at the age of 39 years. He was found to have several small calculi in the left kidney and was discharged on conservative therapy. His blood pressure was 130/88 mm Hg. The patient returned again in 1939 with the history that in February 1938, he had undergone exploration of the right kidney by error and at the same time removal of the stones from the left kidney. Shortly thereafter he began to have severe frontal headaches and intermittent drainage of urine from a sinus tract in the region of the right lumbar scar. Examination revealed hypertension of 180/126 mm Hg and marked eye ground changes. X-rays showed two stones remaining in the left kidney and a marked hydronephrosis on the right due to a ureteropelvic junction obstruction. He failed to respond favorably to repeated ureteral dilatations and periods of indwelling catheter in the right ureter. Prior to nephrectomy his systolic blood pressure varied from

TABLE 1 Hypertension in surgical renal disease

DISEASE	TOTAL NEPHRECTOMY PATIENTS	HYPERTENSIVES	
		Patients	Per cent
1 Tumors			
1) Adenocarcinoma	23	13	56.5
2) Total	39	18	46.1
2 Chronic atrophic pyelonephritis	5	2	40.0
3 Calculus pyonephrosis	77	28	36.3
4 Hydronephrosis	71	18	25.3
5 Chronic pyelonephritis with stone	98	22	22.4
6 Tuberculosis	19	4	21
7 Chronic pyelonephritis without atrophy	3	0	0
8 Miscellaneous	4	0	0
Total	316	92	29.1

150 to 206 mm Hg and his diastolic pressure from 90 to 130 mm Hg. Two months after admission the right kidney was removed. The day before nephrectomy the blood pressure was 156/110 mm Hg and the morning of surgery, under heavy sedation, 180/110 mm Hg. During his 22 days postoperative hospital course his systolic blood pressure varied from 120 to 144 mm Hg, averaging about 130 mm Hg. His diastolic pressure varied from 70 to 110 mm Hg, averaging about 90 mm Hg. His headaches disappeared and eye ground changes regressed. He has been seen on repeated occasions for follow-up study. In 1944 his blood pressure was 130/80 mm Hg and in 1946, 135/75 mm Hg. Eye grounds are now normal. This hypertension evidently developed coincidental with the hydronephrosis due to the ureteropelvic junction obstruction which followed surgery.

Reports indicate that renal infection plays an important role in producing hypertension. The present study shows that 75 per cent of the hypertensive and 78 per cent of the normotensive patients had infection in the removed kidney. It is not surprising that this type of lesion constitutes such a high percentage

ROLE OF PROTECTIVE URINARY COLLOIDS IN PREVENTION OF RENAL LITHIASIS

ARTHUR J BUTT

The formation of urinary calculi is a complex process that is imperfectly understood. They are composed of matter present in two conditions, namely, crystalline and colloidal.* As both crystalloids and colloids enter into the composition of all true calculi, it may be assumed that both of these materials are necessary for the production of a stone. Thus a urinary calculus may be defined as a concretion formed of urinary crystalloids bound together by and incorporated in a colloidal matrix.

Most investigations concerning prevention and treatment of stone have been directed toward trying to diminish the concentration of crystalloids excreted in the urine. With the exception of correcting certain metabolic disorders, these attempts to control calculous formation have not been entirely successful. Our efforts have been focused upon preventing the precipitation of colloids and thus indirectly diminishing the formation of urinary deposits. The influence of colloids in the etiology of stone has hitherto not received the attention it deserves. It is possible that when their action has been studied more fully, we may be in a position to combat the formation of urinary concretions with much greater success.

The ultramicrocosm of the colloids is the twilight between chemistry and physics. Many principles of colloids have been known and applied for centuries, but it was Thomas Graham¹ in 1861 who laid the scientific foundation for colloid chemistry. In 1915, Wo Ostwald² spoke of the colloids as "the world of neglected dimensions." v Buzagh³ in 1927 remarked that the colloids should be more accurately termed "the world of dimensions we may no longer neglect."

Colloids or material in a state of colloidal dispersion are in a position between the microscopic and molecular systems. Colloidal particles are aggregates of large numbers of molecules. Their dimensions are considered to range from 0.001 μ to 1 μ (10^{-7} to 10^{-4} cm). A colloidal solution is clear to the naked eye or when examined using the ordinary type microscope. It is necessary to view the colloidal particles by reflected light rather than by transmitted light because their dimensions are less than the wave length of visible light. The luminosity of the path of a beam of light is caused by the Faraday-Tyndall effect, and it may be considered as an indication of the presence of suspended particles providing the luminosity is not caused by fluorescence. Material in a colloidal state exhibits this phenomenon when transcended by a powerful beam of light.

Read at annual meeting, Southeastern Section, American Urological Association, Memphis, Tenn., March 7, 1951.

* The term "colloid" is derived from the two Greek words "kolla" meaning glue and "eidos" meaning alike.

¹ Graham, T. Liquid diffusion applied to analysis. Phil. Trans. Roy. Soc. 161, part 1, 183-224, 1861.

² Ostwald, W. Die Welt der vernachlässigten Dimensionen. Dresden: T. Steinkopff, 1927.

³ v Buzagh, A. Kolloidik, Dresden: T. Steinkopff, 1936.

motensive nephrectomies 35 years. The hypertensive nephrectomy patients average 9 years older than the normotensive. Of more striking significance is the per cent of patients over 50 years of age in the various groups. Seventy-four, or 24 per cent, of the 316 nephrectomies are over 50 years of age. Of the 92 hypertensive nephrectomies 39 or 43 per cent are over 50 years. Among the 224 nonhypertensive patients there are only 35 or 16 per cent over 50 years of age. Therefore, it is concluded that age plays a significant part in increasing the incidence of hypertension in patients with surgical renal disease.

RESULTS

Sixty-seven of the 92 hypertensive nephrectomies have been followed for 2 or more years after operation. Of the 25 remaining patients, 8 died prior to 2

TABLE 2 *Two years post-nephrectomy results*

DISEASE	TOTAL PATIENTS WITH KNOWN RESULTS	NORMAL BLOOD PRESSURE	
		Patients	Per cent
1 Tuberculosis	2	2	100
2 Hydronephrosis			
1) with infection	11	7	64
2) without infection	2	1	50
3) total	13	8	62
3 Chronic atrophic pyelonephritis	2	1	50
4 Tumors	7	2	29
5 Pyelonephritis with stone	19	5	26
6 Calculus pyonephrosis	24	5	21
Total	67	23	34.3

years after nephrectomy and of 17 we have no postoperative data. The deaths were due to metastatic carcinoma in 5 patients, hemorrhage from gastric ulcer in 1, and cardiac failure in 2. Fifty-five patients have been followed for more than 5 years and 13 over 10 years.

Twenty-three or 34.3 per cent of the 67 patients with good follow-up records had a normal blood pressure two or more years after operation.

Table 2 shows the results in each disease. Both patients with tuberculosis came to normal, but the cases are too few to draw accurate conclusions. Patients with hydronephrosis, with and without infection, show best response to nephrectomy.

The number of patients with chronic atrophic pyelonephritis are too few to form any comparison with the good results published by other authors.¹ One of the two patients in the present report was normal two or more years after operation.

If one considers those patients who are apparently improved, i.e. show a significant drop in blood pressure two or more years after operation, as showing

¹ Barker, N. W. and Walters, W. Hypertension and chronic atrophic pyelonephritis. Proc. Staff Meet. Mayo Clinic, 15: 475, 1940.

attention to the importance of colloids in stone formation. Since then, many theses pertaining to the etiology of stone have referred to an imbalance of colloids and crystalloids, but there is a marked paucity of information concerning further investigation into this phenomenon.

It has long been known that urine contains small amounts of colloidal matter, however, knowledge of their composition is not complete. They can be obtained by means of long continued dialysis against pure water. The colloids obtained in this manner are a mixture of a large number of different substances of which mucin, nucleic acid, chondroitin-sulfuric acid, glycogen, and a complex carbohydrate containing nitrogen have been found.⁶ The total amount of urinary colloids possibly depends upon the diet. It is thought to be increased in a diet rich in proteins, particularly meat. Urinary colloids are also increased in certain diseases, such as pneumonia, and according to Litchwitz,⁷ there is a great increase in the nonalbuminous colloids in acute or chronic inflammatory diseases of the kidney.

It would seem that colloids are a very important, yet often neglected factor, which should be considered in the study of stone formation. Paradoxical as it appears, these tiny particles are highly important in preventing the conglomeration, agglutination, and precipitation of crystalloids, yet when there is derangement of the colloidal mechanisms, there is produced a substance which may cement the crystalline material into a stone. It is possible that these conditions apply not only to urinary calculi but to all types of calculous formation, whether in the prostate, gallbladder, pancreas, teeth, salivary ducts, and even in the mineral world.

From what is known of the effects of the urinary colloids in increasing the solubility of stone-forming salts, it follows that if this protective power is diminished or abolished, urinary deposits will form more readily. Other conditions such as temperature and the reaction of the urine have a marked influence on the nature of the deposits but probably have none in preventing its formation.

It is known that electrolytes are effective in the precipitation of some colloids. This is of great importance when the factors of dehydration and concentration of electrolytes are being considered. Concentration of urine relatively increases the proportion of electrolytes and decreases the proportion of colloids, thereby increasing their possibility of precipitating. Thus with hydration being an important influence in stabilizing colloidal solutions, exposure of the body to dry heat is often a deciding factor as to whether stones will form in persons who are predisposed to calculous formation. This is due to the fact that some of the more insoluble salts may be precipitated when the urine is concentrated through the loss of water by excessive perspiration, insensible fluid loss, etc. This is believed to explain our observation that the months of May through August are the "stone season" in West Florida (fig. 1). It also may explain the comparative frequency of stones which we observe in northern residents who have recently come to Florida. Dehydration has little effect on those persons in whom the

⁶ Joly, J. S. *Stone and Calculous Diseases of the Urinary Organs*. St. Louis: C. V. Mosby Co., 1940.

It is also higher than that found in a group consisting of all types of surgical renal diseases (13.7 per cent)

In a group of unselected, consecutive hypertensive patients, one can expect approximately a 2 per cent incidence of surgical renal disease. This same incidence will be found in a group of consecutive admissions.

In a group of hypertensive patients, surgical renal lesions appear to be only a small possible contributor (2.2 per cent) to the genesis of hypertension. On the other hand, in a group of patients with advanced surgical renal disease the incidence of hypertension is high (29 per cent). This leads one to believe that such lesions may be the initiating factor in the production of high blood pressure in certain patients.

The incidence of hypertension is highest in those patients with renal tumor. The high incidence in tumor patients appears to be due, in part, to the higher age of these patients.

The high contribution to the total hypertensive patients by the infected kidney is misleading. The infected kidney constitutes an equally high percentage of the nonhypertensive group with surgical renal disease.

No one type of surgical renal disease appears to be associated with a more severe type of hypertension than others.

Sex plays no significant role in determining the incidence of surgical renal disease or hypertension among these patients.

Thirty-four per cent of the hypertensive nephrectomies had a normal blood pressure two or more years after operation.

Patients with hydronephrosis, infected and noninfected, show the best response to nephrectomy. Sixty-two per cent of such patients showed permanent relief of hypertension following nephrectomy.

The incidence of return to normal blood pressure among those patients without evidence of cardiovascular disease was two times greater than among those with evidence of cardiovascular disease.

Statistics show that it is the young, mild hypertensive patient who benefits most from nephrectomy.

COMMENTS

The exact relationship of surgical renal disease to hypertension remains to be solved. That there is some basis for the hypothesis that such a lesion may be the initiating factor in the pathogenesis of certain cases of hypertension is supported by the above results in which 58 per cent of mild hypertensives, 24 per cent of moderate hypertensives and 15 per cent of severe hypertensives came to normotension and remained there after removal of the diseased kidney. If one maintains that all essential hypertension is on a renal basis, then he must contend that those patients who do not come to normotension following nephrectomy must have irreversible secondary changes in other organs, particularly in the opposite kidney. It seems more logical to assume that only certain hypertension is due to surgical renal disease. In others the renal lesion is coincidental.

An analysis of 185 cases of renal lithiasis observed by us during a period of two years in West Florida revealed that there were only 4 or 2.2 per cent who were Negroes. Approximately 10 per cent of patients seen by us are Negroes. Renal and ureteral stones are considered as one disease since ureteral calculi are presumably all formed primarily in the kidney. Excretory radiographic studies are routinely made on all of our private and service patients.

Calculus disease of the upper urinary tract is more common in the male than in the female, the ratio varying from 1.2 to 1 to 3.4 to 1. In our series of 185 cases of renal calculi, there were 121 male and 64 female patients, about twice as many men as women. It was further noted that 23 or 36 per cent of these women were nulliparous. Patients 18 years of age or younger were excluded from this series. Physiological changes of the urinary tract, accompanying and following pregnancy, are present from 8 to 12 months, and the average woman has 2.5 children and an even greater number of pregnancies. This means that physiological dilatation and stasis of the urinary tract, often complicated by infection, is present for a period of 20 to 30 months. Analysis of 13,000 obstetrical cases revealed only 8 or .06 per cent complicated by stone. Also excluding the direct effect of pregnancy, women are more prone to have chronic upper urinary tract infection than men. From these facts it would appear that if stasis and infection are the predominant predisposing factor in stone formation, women should have more renal calculi than men. This, however, is not true. With evidence that renal lithiasis is less common in the Negro race than in the white race and less common in the female sex than in the male sex, and with our results of laboratory data indicating marked differences in urinary colloidal activity in these groups,¹⁵⁻¹⁷ one must consider the possible role of "protective colloids" in the prevention of stone.

METHOD OF STUDY

Specimens of urine were obtained aseptically after cleansing the external genitalia. Female patients were catheterized to obtain the specimen, and in male patients specimens were obtained from the second glass of a two glass test. The specimens were collected in two parts. Ten cubic centimeters of urine were placed in a sterile test tube to which was added 0.25 cc of a 25 per cent phenol solution. The tube was stoppered, and the contents of the tube were shaken briskly. The second part of the specimen was centrifugalized and then tested for pH and examined chemically for albumin and sugar. Wet sediment was examined microscopically for erythrocytes, pus cells, yeasts, fungus, and crystals. The sediment was transferred to a slide, fixed with heat, stained with methylene blue, and examined for pus and bacteria. Specimens were discarded if bacteria, leukocytes, erythrocytes or albumin were present. The first specimen was used

¹⁵ Butt, A. J. Discussion of paper, Some Urological Complications of Pregnancy by Drs. Coplan, Woods, and Melvin, Trans. Southeastern Section, American Urological Association, 1950, p. 76.

¹⁶ Butt, A. J. Role of protective urinary colloids in prevention of urinary calculi. Read before Alton Ochsner Medical Foundation, Annual Fellows Meeting, New Orleans, La., Oct. 13-14, 1950.

¹⁷ Butt, A. J. Influence of protective urinary colloids in the prevention of renal lithiasis. J. Fla. Med. Assn. 37: 711-713, 1951.

RECENT TRENDS IN NEPHRECTOMY

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It appeared interesting to analyze records of patients given benefit of nephrectomy during the last 20½ years in order to determine the principal problems confronting these patients and their urologists and to obtain some indication as to the effectiveness of management in regard to 1) the prevention or control of disease processes which may necessitate nephrectomy, 2) the utilization and improvement of available urologic diagnostic facilities and 3) improvement of preoperative and postoperative care. The records of patients hospitalized at the Hotel Dieu Sisters' Hospital and at the Southern Baptist Hospital in New Orleans from January 1, 1930 through June 30, 1950 were searched. Four hundred and thirty-three records were found of private patients for whom nephrectomies were performed. Of the patients admitted to Charity Hospital of Louisiana at New Orleans over the same period of time 707 records were found. The total cases were 1,140 during 20½ years. For comparative analysis, these cases have been divided into four periods: those from 1930 through 1934, from 1935 through 1939, from 1940 through 1944, and from 1945 through the first 6 months of 1950 (fig. 1).

It would be well to recall some of the advances which have been made during these respective periods. From 1930-34 antibacterial agents were limited. In the 1935-39 period the first of the sulfonamide drugs became available. However, their use in this locality was limited until after 1940. Penicillin was available in adequate quantities after 1945. During this period the use of various sulfonamides, streptomycin, aureomycin, chloromycetin and terramycin was begun. In the New Orleans area, though blood could be made available by individual donors, its availability from blood banks was not common until during the 1940-44 year period. Throughout these periods there has been a progressive increase in the number of trained urologists practicing in this city. It is notable that during the last 10 years practically all nephrectomies performed in New Orleans have been done by men trained in urology or by resident urologists under proper supervision.

From the first graph it is notable that there has been a progressive increase in the number of nephrectomies performed during each of these periods (fig. 1). When this increase is compared with the progressive increase in total hospital admissions in the private hospitals under consideration, it would appear that there is some correlation between the total number of nephrectomies and the increase in hospitalization of cases. This is no doubt related to the fact that there has been an increase in the desire for hospitalization by patients and an increase in the utilization of the diagnostic facilities of hospitals. In other words, it indicates that more patients who have need for nephrectomy are now receiving

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no toxic effects Sixty-one series of examinations on urine specimens from 34 subjects were examined for degree of colloidal activity before injection of hyaluronidase, and this was used as control levels Two hundredths milligram (150

TABLE 1 *Comparison of degree of colloidal activity (C A) in Negro and white subjects (114 cases)*

	GRADE C.A.	NUMBER SUBJECTS	PER CENT
Negro	0	0	0
	1—	4	7 1
	1	13	22 8
	2, 3, 4	40	70 1
White	0	3	5 2
	1—	9	15 8
	1	21	36 9
	2, 3, 4	24	42 1

TABLE 2 *Comparison of degree of colloidal activity (C A) in pregnant and nonpregnant women (188 cases)*

	GRADE C.A.	NUMBER WOMEN	PER CENT
Pregnant	0	0	0
	1—	3	4 3
	1	12	17 4
	2, 3, 4,	54	78 3
Nonpregnant control	0	2	2 9
	1—	9	13 1
	1	27	39 1
	2, 3, 4	31	44 9

TABLE 3 *Comparison of degree of colloidal activity (C A) in white males and females (186 cases)*

	GRADE C.A.	NUMBER SUBJECTS	PER CENT
Women	0	2	3 0
	1—	9	13 2
	1	26	38 2
	2, 3, 4	31	45 6
Men	0	3	4 4
	1—	17	25 0
	1	25	36 8
	2, 3, 4,	23	33 8

TRU) of wydase®* dissolved in one cubic centimeter of saline, was injected subcutaneously into these subjects, and colloidal activity of the urine was observed at intervals of 10 minutes, 30 minutes, 1 hour, 2 hours, 24 hours, 48 hours, 72 hours, and 96 hours In 28 or 82 per cent of subjects, colloidal activity was

* Hyaluronidase (Wydase®) was generously supplied by Wyeth Laboratories, Philadelphia

tion In this group of patients, the most common disorder was pyelonephritis. It was found that 203 out of a total of 311 cases had associated calculi. Stag-horn calculi were most commonly found in this group. The second most frequent cause of renal destruction was hydronephrosis (275 cases). Less than half of these cases were found to have associated renal or ureteral calculi. Two hundred and twenty cases had renal destruction primarily due to suppurative disease,

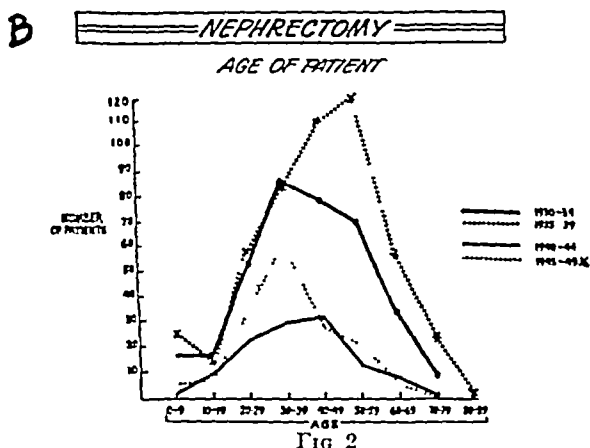
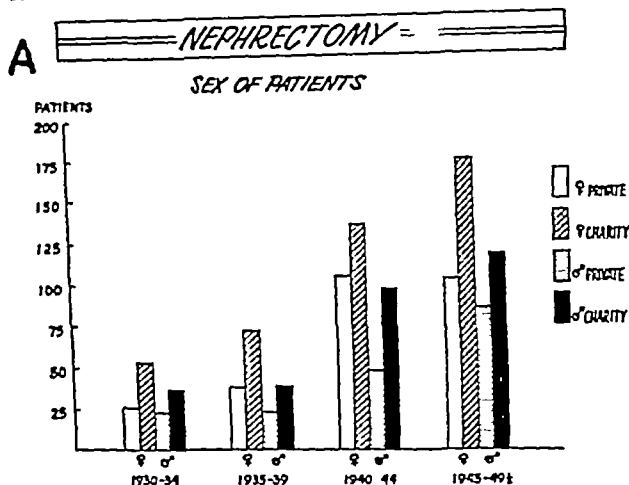


FIG 2

pyonephrosis. There were 155 carcinomas, 57 cases of tuberculosis, 47 cases due to trauma (26 of which were surgical), 24 cysts of the retention type, and 23 cases in which persistent hematuria was recorded as a primary cause for nephrectomy. When one compares these cases of hematuria with the total number of nephrectomies, it becomes evident that they comprise about two per cent. Many of these kidneys would have been saved by more careful study, for included here are only those cases without major renal disease. It would appear that one is more apt to find a persistently hematuric kidney without marked disease in the younger patient. Certainly in the patient below 35 years of age

in number of particles or in motility of the colloid. Two subjects showed no increase in the number of colloidal particles but a great increase in motility of the colloidal particles. Interestingly, the patients who showed no increase in number of colloidal particles harbored renal calculi. A striking observation was that urine from patients who had received hyaluronidase did not sediment as is usually the case. Colloidal activity in these urine specimens was elevated for several days and then returned to normal. Some specimens kept in sealed test tubes remained clear indefinitely after injection of hyaluronidase (fig. 2).

The group of 28 subjects with positive response to hyaluronidase were analyzed. Urine specimens from 5 Negro subjects, without stone, showed grade 1 plus activity before injection, and after injection, activity increased to an average of grade 3 to 4. Urine from 8 white subjects, without stone, whose initial specimen showed grade one colloidal activity, after injection of hyaluronidase, colloidal activity increased to an average of grade 2 to 3. Urine specimens from 15 patients with stone whose initial colloidal activity was grade 1 minus, following injection of hyaluronidase, the activity became elevated to an average of 2 to 3 (fig. 3). When hyaluronidase is added directly *in vitro* to urine specimens and incubated from 1 to 6 hours, there is no significant change in colloidal activity.

DISCUSSION

The origin of urinary colloids is still obscure. It has been suggested that they are derived from the renal epithelial cells.⁹ From our observations that injection of hyaluronidase increases colloidal activity and does not change the colloidal activity in urine specimens in which the hyaluronidase is added *in vitro*, the fact that approximately ten minutes elapses between the time of injection and appearance of the first change in increase of colloidal activity and remains elevated for hours leads us to believe that hyaluronidase or one of the products it releases acts as a primary factor in the production of protective colloids. The exact mechanism is not yet known. Further investigation in this field is being carried out in collaboration with Dr. Ernst A. Hauser and the Wyeth Institute of Applied Biochemistry. We have observed that urinary colloids are increased in patients with acute and chronic inflammatory diseases of the kidney which may favor their renal origin. We have also noted that patients with chronic glomerulonephritis and patients who are chronic alcoholics rarely develop renal calculi. In inflammatory conditions of the kidney, colloids are often precipitated in the form of tube casts. It is believed that hyalin casts are merely masses of colloids which have set in the form of a "gel."

There are two types of colloids: lyophilic and lyophobic. The lyophilic colloids are highly solvated and owe their stability primarily to their affinity toward the dispersion medium. The lyophobic colloids, being poorly solvated, owe their stability primarily to the electrical charge of the individual dispersed particle. Lyophilic colloids, after being precipitated, may be brought back to their original state of dispersion without great difficulty. Lyophobic colloids, after being precipitated, cannot be brought back to the original degree of dispersion without drastic chemical and/or physical means. When lyophilic colloids are mixed with

TRAUMA

During recent years practically all major accident cases in New Orleans have been initially carried to the Charity Hospital because of faster ambulance service. Since the majority of cases requiring nephrectomy because of external injury necessitate operation within a matter of a few hours and since these patients have been too ill to be moved, they were found among the charity cases (7 per cent charity, 15 per cent private, 1945-49½). Like the malignancies, the abnormally high percentage (10 per cent) in the earliest period is accounted for by the small total number of cases during this period, which is in turn due to the lack of hospitalization and application of diagnostic methods in recognition of other conditions necessitating nephrectomy.

Of the total of 47 cases in which the kidney was removed primarily because of trauma, 26 cases were due to surgical injury. Twenty of these occurred to the ureter at the time of pelvic surgery. Such injuries have been more common during the last 5 years because of 1) the increased utilization of radical pelvic surgery for carcinoma of the cervix, 2) the increased number of abdomino-perineal resections for malignancy of the rectum and sigmoid colon and 3) the increased removal of large ovarian or uterine tumors with displaced ureters. On 6 occasions an attempt was made to remove stones from the kidney and bleeding and injury to the renal parenchyma were such that it was deemed advisable to remove the kidney.

TUBERCULOSIS

Since during the last 3 periods under consideration tuberculosis accounted for 3 per cent, 5 per cent, and 2 per cent of private and 25 per cent, 45 per cent, and 3 per cent of charity patients nephrectomized, it would appear that there has not been a definite decrease in the nephro-ureterectomy for tuberculosis in spite of better control of spread and improved therapy for tuberculosis in general. It is suggested that streptomycin is not the answer to the question of definitive therapy of renal phthisis.

PYONEPHROSIS

Though there were a total of 220 cases of pyonephrosis, comparison (fig. 4) of these cases with the total number of nephrectomies during the periods under consideration indicates that the condition is being found less common. This would be expected with better application of effective antibacterial agents.

CALCULI

When one peruses table 1 it is evident that we have not done a great deal in solving the problem of renal calculi. Of the patients with hydronephrosis, pyonephrosis and pyelonephritis (a total of 806) the majority had renal or ureteral calculi.

MORTALITY

There were a total of 64 deaths among these 1,140 patients. When one computes percentages of mortality during the five year periods, it is found that both

INTRARENAL LIPOMA REPORT OF A CASE

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Intrarenal lipomas of sufficient size to be of surgical importance are of the rarest of renal tumors. In 1941 Robertson and Hand reviewed the literature, found 12 cases and added 2 cases of their own. In 1949 O'Heeron added a case to bring the total to 15.

The origin of these tumors is of interest inasmuch as the kidney normally does not contain fat. Alsbet believed that they take origin in embryonic fatty rests whereas others think that such tumors could arise from perivascular and intertubular connective tissue which undergoes fatty metamorphosis.

In the cases previously reported, eleven suffered some pain at the site of the lesion. Three patients complained of chronic digestion. Four of the patients had hemorrhage into the substance of the tumor. Pyelographic findings were of interest in that twelve presented changes of the type seen in renal tumors. One patient revealed a stone and the remaining two had normal pyelographic patterns bilaterally.

A case report of intrarenal lipoma is presented in a 52 year old white woman. The history is of special interest in that both the patient and her husband were suddenly taken ill with nausea, vomiting, diarrhea and fever. At the onset of her illness she noted a tender mass in the right upper abdomen and complained of severe pain in the right abdomen and back. Two days after the onset her husband's symptoms disappeared but the patient continued to have nausea, vomiting and temperature up to 100°F daily. After 10 days the acute symptoms subsided. She presented herself for examination because of a persistent tender "lump" in the right upper quadrant. There was no past history of jaundice, biliary colic, chronic indigestion, or urinary symptoms.

The patient weighed 152 pounds. The oral temperature was 99.4°F, pulse was 84, and blood pressure 150/104. The remainder of the physical examination was negative save for the abdominal findings, which revealed a mass approximately 6 by 8 cm. in the right upper quadrant. It seemed to be quite superficial and was very tender to palpation. On manipulation of the mass there was a reference of pain to the back.

The red blood count was 3,590,000 per cubic millimeter, the white blood count was 14,500 per cubic millimeter, hemoglobin was 12 grams per 100 cc. Differential blood count was polymorphonuclear cells 84, lymphocytes 16. The sedimentation rate was 48 mm. by Wintrobe method in 1 hour. Brucellosis agglutination was negative. The hematocrit was 42 per cent packed red blood cells. Stool examination was negative for amoeba. Urinalysis was normal.

The problem presented was that of the differential diagnosis of a right upper quadrant mass. A cholecystogram and barium enema revealed the mass to be separate from both of these organs, however, the colon was depressed by the mass (fig. 1). Following these procedures, cystoscopy was performed. The blad

The lowest mortality was found among the cases where renal destruction was primarily due to hydronephrosis. The mortality for this group was a total of 1.5 per cent. The least common type cases expiring were chronic pyelonephritis with stag-horn calculi, 3 deaths, tuberculosis, 1 death, polycystic kidney with infection, 1 death, and 1 death of an infant in whom the ureter was anastomosed to the subarachnoid space. This patient died several weeks after operation from associated infection.

In appraising the mortality associated with nephrectomy a study was made to determine the principal causes of these deaths (fig 5). Twenty-nine were found to be primarily due to sepsis. Analysis over the 5 year periods revealed that with the increased availability of effective antibacterial agents there has been a marked reduction in such mortality so that now it is less than 1.5 per cent for both the private and charity cases. The second most common cause is shock and hemorrhage. Some patients experience shock due to surgical trauma

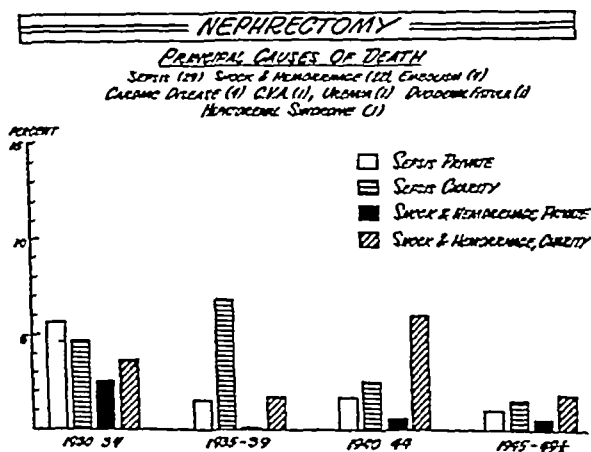


Fig 5

and anesthesia whereas in other instances it is due to blood loss before or at the time of operation. There were 22 such cases. In the overall there seems to be some tendency toward a decrease in these cases of mortality but as compared with the other causes they still remain quite important. This emphasized the necessity of proper preoperative preparation of the patient and adequate utilization of blood before the patient loses too much. Since the deaths from sepsis, shock and hemorrhage have decreased, embolism is playing a larger part. There have been 4 deaths from embolism during the last 10 years. There have been 4 instances in which patients had marked cardiac disease as the primary cause of death. One cerebral vascular accident, 1 instance of renal failure which was not due to shock or hemorrhage, 1 duodenal fistula of a total of 3 cases and 1 hepatorenal syndrome have occurred.

BLOOD ADMINISTRATION

When a study of blood administration was made it became apparent that since blood is readily available in hospital blood banks it is more commonly

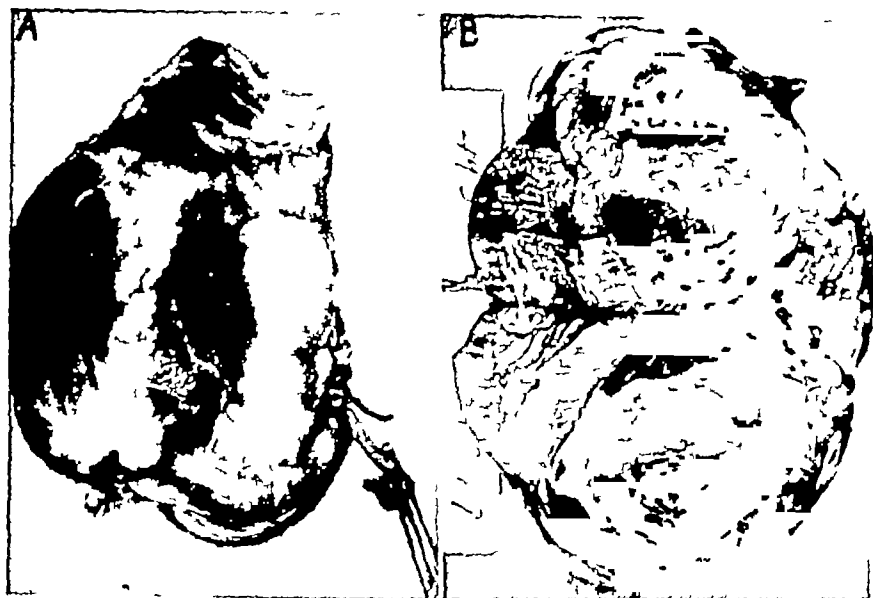


FIG 3 A, gross specimen uncut B, gross specimen cut Kidney below and tumor with large hemorrhagic area, above



FIG 4 Showing fat cells of tumor located in renal parenchyma

Analysis of ages of patients reveals a definite trend toward an older age at the time of nephrectomy

Infection predominates as the primary cause for nephrectomy in spite of a decrease in the frequency of acute suppurative disease

The incidence of calculi in excised kidneys has not decreased in spite of more effective antibacterial agents

Of the patients given benefit of nephrectomy, the percentage of those with renal tuberculosis remains essentially unchanged

Cancer has become a more frequent cause for nephrectomy, but the mortality of renal neoplasm remains too high

Surgical injury of the ureter requiring nephrectomy has been more frequent during recent years

The total hospital mortality has decreased from 10.3 per cent to 4.7 per cent for charity cases and from 8.2 per cent to 2.7 per cent for private cases

The most marked reduction in mortality has occurred in those cases caused by sepsis

Shock and hemorrhage continue to be important causes of death. Better preoperative, operative and postoperative care should add to the trend toward a lower mortality

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SECTION OF THE INFERIOR VENA CAVA FOR RETROCAVAL URETER A NEW METHOD OF TREATMENT

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Retrocaval or postcaval ureter is now a well recognized though rare developmental anomaly, in which the right ureter in its descent to the bladder passes behind the inferior vena cava.

INCIDENCE

Up to 1931 only 10 cases had been reported (Pick and Anson) but 29 have appeared in the literature since then, 20 of which have been operated upon. The fact that only 39 cases have been described is not an indication of the incidence of the anomaly but of our ignorance of its existence. There is no doubt that as the knowledge of the condition becomes more widespread, the diagnosis of postcaval ureter will be made more often.

It appears to be commoner in males than in females and to affect the right ureter almost exclusively. Only 1 case of bilateral postcaval ureters has been traced in the literature, it was described by Gladstone in an acardiac fetus.

EMBRYOLOGY

The embryology of the defect has been fully dealt with by Randall and Campbell, Pick and Anson and Gruenwald and Surks. Only the main facts will be outlined here. The posterior cardinal vein is situated laterally and the subcardinal vein medially in the dorsal part of the urogenital fold. In a more posterior plane are two longitudinal venous channels on either side of the sympathetic trunk, termed the medial and lateral sympathetic veins respectively. The definitive inferior vena cava below the level of the renal veins is normally formed by the right lateral sympathetic vein (right supracardinal vein of Huntington and McClure). The posterior cardinal vein disappears and the infra-renal part of the subcardinal vein becomes the vein of the developing gonad. The metanephros ascends in a plane dorsal to the posterior cardinal and subcardinal veins. Should either of these veins persist to form the infra-renal part of the definitive inferior vena cava, the ureter will obviously be postcaval in position and will follow an abnormal course, depicted in figure 1. Postcaval ureter is thus a defect in the development of the vascular system. It is generally agreed that the fault in postcaval ureter is persistence of the right posterior cardinal vein. Gruenwald and Surks, however, consider that a persistent subcardinal vein forms the pre-ureteric vena cava.

Of more practical importance is the relation of the ureter to the tributaries of the anomalous inferior vena cava in these cases. The normal arrangement of these tributaries is described in the following quotation from a current text of anatomy. The terminations of the lumbar veins are very variable. The upper two on each side may end in the ascending lumbar veins or in the azygos

Siedentopf⁴ in collaboration with Zsigmondy constructed the first "ultramicroscope." Observations with the use of this instrument demonstrated it to be of great value in the investigation of colloidal solutions. When sols, as these solutions are called, are observed with the ultramicroscope, the colloidal particles appear as bright discs in a state of ceaseless, agitated, zig-zig, erratic, rapid motion known as Brownian movement. Brown⁵ stated that the movement of the particles arose neither from currents in the fluid nor from its gradual evaporation, but belonged to the particle itself. It is now known that the movement of the particles suspended in a liquid or gas is due to the actual bombardment of particles by molecules of the continuous phase. It constitutes a visual demonstration of molecular kinetic energy. The apparent size of the bright images bears no relationship to the size of the actual particle. It is possible, however, to count the number of particles in a field of the ultramicroscope and thus determine the number in a known volume of fluid (field diameter approximately 0.002 mm, volume 1×10^{-3} ml). The electron microscope is also available for examining much smaller particles. Practical difficulties, however, limit the utilization of the full theoretical resolving power of the electron microscope.

If the particles of a substance are reduced in size until the dimensions become submicroscopic and are distributed throughout a second medium, they develop characteristic properties attributable to the enormous surface area of the dispersed phase. It has been estimated that 1 gm. of colloidal material in urine has a surface area of approximately 5,000 square meters. One of the most important results of this large surface is the unsaturation of the ions located in the surface, causing adsorption of ions dispersed in the surrounding medium and carrying an electric charge of opposite sign. This leads to the formation of electrical charges around the particles, preventing their collection into larger aggregates. It has been postulated that an electrical layer of ions forms around the colloidal particle, thus acting as an electrical condenser which prevents particles from cohering. Another important factor in preventing precipitation and agglutination of colloids and crystalloids is that sedimentation of finely divided material may be almost entirely counteracted by the Brownian motion of the colloidal particle.

Urine is a supersaturated solution. The abnormal solubility of the stone-forming salts depends upon the presence of certain colloids which prevents precipitation of salts and other colloids. Litchwitz⁶ determined that this protective action of the urinary colloids belongs to a very high order. Rainey and Ord⁷ observed that crystals formed in solutions containing colloids differ from those derived from pure aqueous solution. Ebstein⁸ in 1884 was the first to draw

⁴ Siedentopf, H. *Druckschriften Verzeichnis der optischer werkstaette von C. Zeiss* Berl. klin. Woch., vol. 32, 1904.

⁵ Brown, R. quoted by Hauser, E. *Colloidal Phenomena*. New York: McGraw-Hill Co., 1939.

⁶ Litchwitz, L. *Über die Bildung von Niederschlägen und Konkrementen in Harn und in den Harnwegen*. Kraus, F. und Brugsch, T. *Spezielle Pathologie und Therapie innerer Krankheiten*, 1. Band. Berlin, Urban und Schwarzenberg, pp. 239-296, 1919.

⁷ Rainey and Ord. quoted by Joly.

⁸ Ebstein, W. *Die Natur und Behandlung der Harnsteine*. Wiesbaden, 1884.

lumbar tributary of the abnormal vena cava. In Kimbrough's case the retrocaval ureter passed behind the right common iliac vein as well. The importance of these relationships will be discussed later.

SYMPTOMATOLOGY

The defect may be symptomless. On the other hand, it may cause hydronephrosis with or without infection or stone.

The etiology of the hydronephrosis has been variously ascribed to kinking of the ureter in its abnormal course, stricture of the retrocaval part of the ureter, pressure on the ureter by the inferior vena cava or to a combination of these factors. Several cases of postcaval ureter have been found at necropsy or in the anatomy laboratory without hydronephrosis, so that the abnormal position of the ureter does not necessarily cause obstruction. Because of this, Pick and Anson suggested that another factor, namely nephroptosis, must be present before back pressure develops. They suppose that as the kidney descends, the ureter may be caught up and kinked by a venous crutch of the type they describe. In support of this view, a study of the literature suggests a possible relationship between the level of the kidney on the one hand and the course of the ureter and the degree of hydronephrosis on the other. Those cases with a low-lying right kidney show a ureter with an S shaped rather than a sickle shaped curve and, correspondingly, a greater degree of hydronephrosis.

It was previously supposed that time was an important factor in the development of the hydronephrosis, since all cases of postcaval ureter with hydronephrosis had occurred only in adults (Derbes and Dial, Wilson and Herzlich). This idea is now nullified by Anderson and Hynes who found a well-advanced hydronephrosis in a child of 10.

Greene and Kearns found the retrocaval part of the ureter "thin, pale and inelastic, it did not respond to pinching and was entirely devoid of contractility." They considered that the ureter at this point was fibrotic and had never developed a normal muscular wall. Unfortunately, they give no histological report on the piece of ureter which was excised.

Some authors described the retrocaval part of the ureter as constricted, while others found the ureter of equal diameter throughout. Examination of a portion of ureter removed by Randall and Campbell showed no abnormality except mild inflammation.

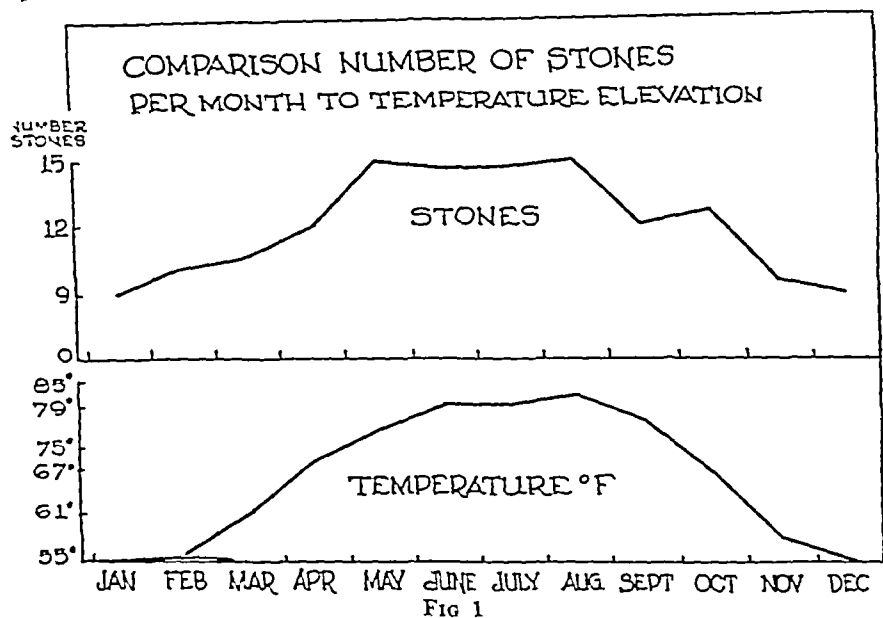
Several writers considered that the inferior vena cava compressed the ureter, although only Anderson and Hynes gave definite proof of this. They found that the renal pelvis emptied on freeing the ureter from the inferior vena cava. The same effect was observed in the present case, leaving no doubt that compression by the inferior vena cava was the only obstructing factor.

Lebelhor noted good peristalsis throughout the retrocaval part of the ureter on stimulating the pelvis. He was certain that in his case the right testicular (internal spermatic) vein, and not the inferior vena cava, was obstructing the ureter.

Young found a calculus impacted at the lower kink in a retrocaval ureter,

colloids are able to maintain the crystalloids in solution. Even if they have poor protective colloidal activity of urine, they might be able to live comfortably in cooler climates, but many will be unable to withstand the increased concentration of urine that occurs in hot climates. In most areas where the climate is damp and hot, there is relative freedom from stone.

Some races are more prone to urinary lithiasis than others. The Negro is relatively immune. Vermooten¹⁰ observed that the South African Negro does not experience the formation of renal calculi. His conclusions are based upon an examination of the records of 1,090,000 Negroes admitted to the Johannesburg Hospital. At the same time, the white population of South Africa, according to



records of 126,000 admissions, had renal calculi in the ratio of 1-460 patients. In Egypt, the Arab shows a greater predisposition to stone than the Negro. Negroes in the United States are less liable to stone formation than the white race. Quinland¹¹ reported only 13 cases of renal lithiasis or 0.8 per cent in 15,919 autopsies and surgical specimens observed during a twenty-two year period in an exclusively Negro hospital. Bell¹² noted that in 24,561 autopsies on all races there were 285 or 1.2 per cent with upper urinary tract calculi. Cary¹³ observed that urolithiasis is more common in white than in Negro patients. Holmes and Coplan¹⁴ have stated that urinary lithiasis in Negroes is rare in South Florida and that the infrequent Negro with renal stone is often a mulatto.

¹⁰ Vermooten, V. Occurrence of renal calculi and their possible relation to diet as illustrated in South African Negro, J.A.M.A., 109: 857, 1937.

¹¹ Quinland, W. S. Urinary lithiasis, review of 33 cases in Negroes J. Urol., 53: 791, 1945.

¹² Bell, I. T. Renal Disease. Philadelphia: Lea and Febiger, 1946.

¹³ Cary, M. R. Racial incidence of urolithiasis J. Urol., 33: 651, 1937.

¹⁴ Holmes, P. J. and Coplan, M. M. Study of geographic incidence of urolithiasis with consideration of etiological factors J. Urol., 23: 477, 1930.

Several surgeons who did not resect a piece of ureter considered nephropexy necessary. Nephropexy was also done by Lowlsley, even after removing about

TABLE 1 *Analysis of treatment*

AUTHOR	METHOD	COMPLICATIONS	END RESULT
1 Kimbrough 1935	1 Nephropexy and renal sympathectomy 2 Ureteric section + re-anastomosis	—	Narrowing of ureteropelvic junction required dilatation
2 Rotter 1935	Nephrolithotomy for calculi	—	Died
3 Randall & Campbell 1935 (2 cases)	1 Subcapsular nephrectomy 2 Nephrectomy	—	—
4 Uebelhör 1936	Ureteric section and re-anastomosis + nephropexy	—	Sinus? from ureteric stump Said to be good but no post-operative pyelogram shown.
5 Derbes & La Nasa 1937	Nephrectomy for calculi	—	—
6 Shih 1937	Nephrectomy	—	—
7 May 1938	Ureteric section and re-anastomosis + nephropexy	—	Satisfactory
8 Harrill 1940	Section above ureteropelvic junction and re-anastomosis	Infection	Satisfactory
9 Harbach 1940	Nephrectomy for severe renal damage	—	—
10 Wilson & Herzlich 1944	Nephrectomy	—	—
11 Goyanna et al 1946	Ureteric section excision of a segment of ureter + re-anastomosis	—	No mention of infection or stricture after operation
12 Lowlsley 1946	1 Section of ureter outside bladder. Ureter removed from behind vena cava and reimplanted into bladder. Nephropexy	2 Operation for stricture 3 cm above site of reimplant after 6 weeks	Abscess formation and sloughing at lower end of ureter 3 Skin nephrostomy
13 Nourse & Moody 1946	1 Ureteric section + re-anastomosis	Delayed healing of nephrostomy wound Calcification at anastomosis Infection 2 Attempted repair of ureter	3 Nephrectomy 5 months later
14 Creene & Kearns 1946	Ureteric section + re-anastomosis excluding postcaval ureteric segment. Kidney lowered	Leakage at anastomosis Infection	Regular ureteric dilatation planned
15 Young 1947	Removal of ureteric calculus	—	Satisfactory
16 Creevy 1948	Ureteric section + re-anastomosis via transperitoneal and lumbar incisions	Ureteric dilatation for 3 months	Development of stricture feared
17 McElhinney & Dorsey 1948	Ureteric section + re-anastomosis with excision of constricted segment of ureter	Infection. Repeated ureteric catheterization	Possible stricture formation
18 Anderson & Hynes 1949	Excision of redundant pelvis ureteropelvic junction and upper ureter. Anastomosis of ureter to pelvis. Modified nephropexy	—	Satisfactory
19 Shearer 1949	Ureteric section + re-anastomosis. Nephropexy	—	Stricture requiring dilatation

6 cm of the lower end of the ureter. Kimbrough tried nephropexy and renal sympathectomy alone, but later resorted to ureteric section and re-anastomosis. Creevy exposed the retrocaval part of the ureter by a transperitoneal approach and anastomosed the cut ends of the ureter through a lumbar incision. He

for studying "colloidal activity" This was examined under the microscope using high dry lens (X 440) with dark field attachment One drop of immersion oil was placed on the dark field condenser A clean slide was placed in position above the condenser, and the condenser was then elevated until oil made contact with the glass slide One drop of urine was transferred from the test tube by means of a new, clean, wooden applicator stick to the center of the glass slide, and this was covered with a clean cover glass The microscope was adjusted until Brownian motion was observed Particles exhibiting Brownian motion were considered as evidence of inherent colloidal activity in the specimen as all extraneous matter, dust, small bacteria, albumin, fragmenting leukocytes or erythrocytes, and other artifactual materials which could produce Brownian motion were excluded Electrophoretic studies of urine samples were performed by Dr Ernst A Hauser, professor of colloid chemistry, Massachusetts Institute of Technology and Worcester Polytechnic Institute He found that the colloids all carry a net negative charge and that by their electro-kinetic potential they are protective colloids As the degree of "colloidal activity" (increase in number of colloidal particles) increases, there is a lessening of agglomeration and a pronouncedly slower migration in the electric field, indicating a more effective protective action

RESULTS OF EXAMINATION OF URINE FOR COLLOIDAL ACTIVITY

Colloidal activity was graded from zero to four, zero representing no colloidal activity, grade 1 minus, one to two colloidal particles intermittently present in the field, grade 1, one to five particles constantly present in the field, grade 2, six to ten particles per field, grade 3, eleven to twenty particles per field, and grade 4, over twenty particles per field Four hundred sixty-two specimens of urine were examined Grade 1 colloidal activity was found to be the norm Grade 1 minus was considered as reduced colloidal activity, and grades 2, 3, and 4 were considered as elevated colloidal activity

Colloidal activity in urines from Negro and white subjects without stones revealed that the former had a much higher degree of colloidal activity than the latter (table 1) The only urine specimen from a Negro that showed zero colloidal activity was one who harbored a renal stone Urine specimens from pregnant women constantly showed a higher degree of activity than that from nonpregnant women (table 2) A ureteral calculus was present in the only pregnant woman whose urine showed zero colloidal activity It was found that women generally have a higher degree of colloidal activity than men (table 3) Urine from patients with renal calculi displayed significantly lower colloidal activity than the control group without stones (table 4)

Studies were then undertaken in an effort to find a method of increasing the protective urinary colloids The spreading properties of hyaluronidase suggested that this drug might be useful for this purpose¹³ "Hyaluronidase has practically

¹³ Duran Reynolds F Tissue permeability and spreading factors in infections *Bact Rev* 6 197-199, 1942

¹⁴ Scifter J Studies in the pharmacology and toxicology of testicular hyaluronidase *Ann New York Acad Sci*, 62 1141-1155, 1950

A plain film revealed no evidence of urinary tract calculi. A provisional diagnosis of pyelocystitis was made and a course of sulfathiazole prescribed. He was seen at intervals for the next 2 months and on each visit the urine contained an occasional leukocyte and a moderate number of erythrocytes but was sterile on culture. The pain in the right loin persisted, however, and an excretory urogram revealed hydronephrosis of a moderate degree on that side. The right ureter was not visualized. The left renal pelvis and ureter were normal.

In view of this finding he was referred to Mr Hugh Donovan for further investigation. On admission to the Queen Elizabeth Hospital, Birmingham physical examination revealed a palpable right kidney but no other abnormality. The blood urea level was 49 mg per 100 ml. A urea concentration test gave

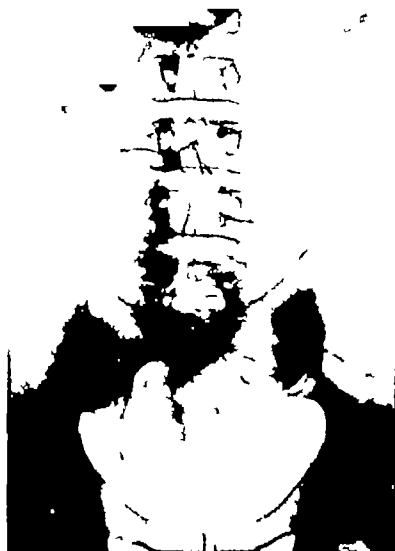


FIG 2 Preoperative retrograde pyelogram showing degree of hydronephrosis and course of ureter

values of 2 per cent, 2.9 per cent and 3 per cent. Urinalysis showed no pus cells, a moderate number of erythrocytes and a nonsignificant growth. On cystoscopy the bladder was normal. The right ureteric orifice was horseshoe-shaped and appeared relaxed. The comment on it was "it would pass for a large normal." A No. 10 Beniqué ureteric catheter passed easily up the right ureter for 22 cm at which point it was checked. The pyelogram (fig 2) showed a characteristic appearance. From the pelvic brim the catheter passed obliquely upwards to the left across the front of the bodies of the fifth and fourth lumbar vertebrae, reaching almost to the midline at the upper border of the fourth lumbar vertebra. It then curved gradually to the right with a convexity directed upwards and to the left. The tip of the catheter was seen pointing horizontally to the right in front of the transverse process of the third lumbar vertebra, a short distance below the ureteropelvic junction. Calyceal hydronephrosis and dilatation of the upper fourth of the ureter can also be seen. A diagnosis of postrenal ureter

TABLE 4 Comparison of degree of colloidal activity (C.A.) in patients with renal calculi and control group (74 cases)

	GRADE C.A.	NUMBER SUBJECTS	PER CENT
Patients with stones	0	6	16.2
	1-	8	21.6
	1	17	46.0
	2, 3, 4	6	16.2
Patients without stones			
Control	0	1	2.7
	1-	4	10.8
	1	17	46.0
	2, 3, 4	15	40.5



FIG. 2 Comparison of urinary sediment before and after parenteral administration of hyaluronidase. Specimens allowed to sediment for 14 days. A control before administration of hyaluronidase. B specimen collected 2 hours following administration of hyaluronidase.

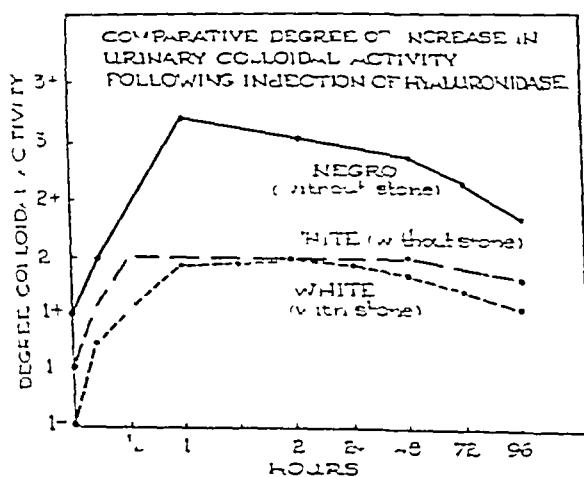


FIG. 3

significantly increased following injection of hyaluronidase. It was found that the activity began to rise in 10 minutes and reached a peak in from 1 to 2 hours. Activity remained elevated for 24 to 96 hours. Four subjects showed no increase

was no edema. Two days later most of the venous congestion had disappeared. Convalescence was marred by pyrexia and gaseous distension of the abdomen with constipation. The temperature returned to normal and the ileus subsided gradually during the next 2 weeks. A well marked superficial venous collateral



FIG. 4 Excretory urogram 3 months after section of inferior vena cava



FIG. 5 Absence of edema of legs 6 months after section of inferior vena cava

circulation developed, as shown by infra-red photographs taken 3 weeks after operation (fig. 3). On the eighteenth post-operative day the patient was found to have a thrombosis of the right long saphenous vein as far down as the knee, associated with pitting edema. At this time the urine contained red cells and an occasional pus cell, but remained sterile. As no other cause for the pyrexia could be found, it was attributed to the absorption of thrombus. He was dis-

lyophobic colloids, the latter becomes lyophilic in properties because its surfaces have been coated with lyophilic colloids. This is attributed to the formation of a film of lyophilic colloid over the lyophobic colloid. There is evidence that physicochemical changes resulting from the effects of dehydration and discharge of electrical potentials around the particle, due to as yet unknown factors, which change the lyophilic colloid into a lyophobic colloid. The lyophobic colloids may become deposited on a renal papilla or sediment to the most dependent part of a calyx or pelvis and there acts as a gluing or cementing substance which holds the crystalloids together and thus aids in the formation of a urinary calculus.

CONCLUSION

A clearer understanding of the urinary colloids helps explain in more basic physicochemical terms why adequate hydration is exceedingly important in the prevention and treatment of urinary calculi.

A better knowledge of the colloids may lead to a method of detecting which persons have a greater or lesser predisposition to the formation of urinary calculi.

There appears to be a definite correlation between the fact that the colloidal activity is elevated in the Negro race as compared to the white race, and that the former is less liable to stone formation than the latter.

Observation of elevated colloidal activity in pregnant women offers an explanation as to why pregnancy which is so often associated with dilatation and stasis of the urinary tract and increased excretion of calcium is not more frequently complicated by urinary calculi while nulliparous women are relatively less prone to calculous formation than their parous sisters.

The fact that patients who harbor renal calculi have decreased urinary colloids leads us to believe that reduction or absence of these protective colloids have a definite bearing on the formation of stones in these patients.

Following injection of hyaluronidase in various groups of patients revealed that colloidal activity is significantly increased in 82 per cent of subjects. The greatest response was in members of the Negro race. There was less response in white persons without stones. The least response was in patients who harbored renal calculi. Of great interest was the observation that urine specimens from patients who had received hyaluronidase did not sediment for long periods of time as compared to urines from the same subjects before they had received hyaluronidase.

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the vena cava is bilateral, the left common iliac vein fails to join the right. It is also possible that section of tributaries of the inferior vena cava may be all that is needed in some cases to allow the ureter to function properly. It is a pity, for instance, that section of the testicular vein was not tried in Uebelhör's case.

The ideal to be aimed at in all corrective surgery is the restoration of normal anatomy and function wherever possible. Although section of the inferior vena cava produced an excellent result in this case, an attempt at re-anastomosis of the vein by a suture method should be worth while. This might obviate the deep vein thrombosis which is known to occur below the site of ligation of the inferior vena cava, even in the absence of thrombosis before operation. But if the uncertainties of vein anastomosis could not be risked, simple section of the vein might be preferable.

Regarding the choice between an attack on the ureter or on the inferior vena cava, there can be no doubt that the caval operation is preferable when the other kidney is severely damaged or functionless, as in Lowsley's case.

Finally, it is tentatively suggested that before ureteric section is decided upon, the ureter should, if possible, be thoroughly freed from the inferior vena cava, cutting any obstructing tributaries of that vein if necessary. Should satisfactory peristalsis then be seen, the case is eminently suitable for section and re-anastomosis of the inferior vena cava. If plastic repair of the ureter is preferred, the pelvic methods of Harrill or Anderson and Hynes appear to be better than end-to-end anastomosis of the ureter. If, however, a ureteric stricture is present, or if the ureter is firmly embedded in the wall of the vein, such methods are obviously contra-indicated and end-to-end anastomosis of the ureter may be the only course left to the operator, apart from nephrectomy.

SUMMARY

Posterior ureter will be more frequently diagnosed as the knowledge of the condition becomes more widespread.

The diagnosis is easy when the characteristic radiographic appearances are known.

In some cases, compression of the ureter by the abnormal inferior vena cava or its tributaries is the sole cause of the associated hydronephrosis.

All the cases in the literature which have been treated surgically are analyzed. The disadvantages of plastic operations on the ureter are obvious.

The choice of treatment is between nephrectomy and operative correction.

When pressure on the ureter by the inferior vena cava is the only obstructive factor present, section of the inferior vena cava is a more rapid and certain method of relief than section and re-anastomosis of the ureter.

Section of the abnormal inferior vena cava or its tributaries is certainly the method of choice when the opposite kidney is functionless, when the infrarenal vena cava is bilateral or when there are two inferior venae cavae on the right side and the ureter passes between them.

It is suggested that, in future, re-anastomosis of the inferior vena cava might be attempted.

der was normal and the ureters were catheterized with ease. The function of both kidneys as measured by indigo carmine was within normal limits. The appearance time of the dye was 3 minutes on the left and $4\frac{1}{2}$ minutes on the right, with



FIG. 1. *A*, cholecystogram and plain urogram showing mass separate from gallbladder. *B*, colon x-ray showing depression of hepatic flexure by mass.

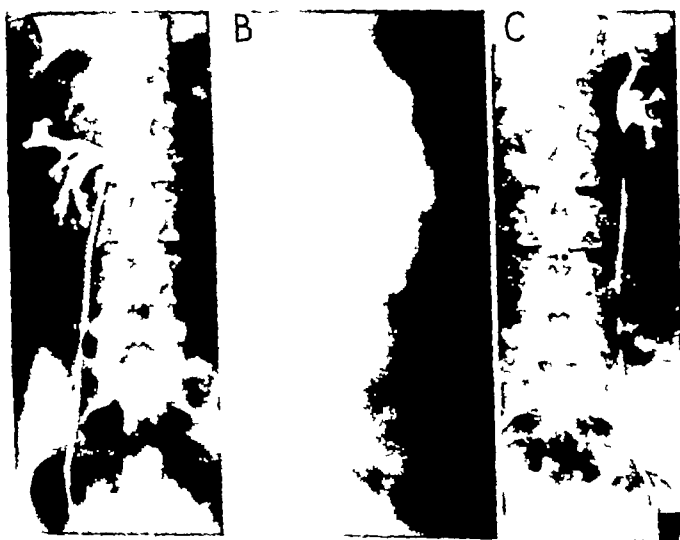


FIG. 2. *A*, right pyelogram, anteroposterior view. *B*, right pyelogram, oblique. *C*, left pyelogram, anteroposterior view, compare with right.

x-ray plus concentration bilaterally. Retrograde pyelograms were taken in the anteroposterior, oblique, and true lateral positions (fig. 2).

At operation a large tumor involving the right kidney was found. A right nephrectomy was done which included the tumor. The patient's postoperative course was uneventful and she was discharged from the hospital on the seventh postoperative day.

RADIOTHERAPY IN THE TREATMENT OF NONSPECIFIC INFLAMMATORY STRICTURE OF THE URETER

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Prior to the advent of the newer chemotherapeutic and antibiotic agents, radiotherapy was frequently used in the treatment of a variety of superficial and deep infections. When the efficacy of these newer agents was established the need for radiotherapy in infections became less frequent. The purpose of this paper is to demonstrate a beneficial effect from the use of x-ray therapy in a case of nonspecific inflammatory obstruction of the ureter. Previous treatment with surgery and antibiotics had been unsuccessful.

CASE REPORT

I W, a 57 year old white man, presented himself on May 5, 1949 with a history of right pubic pain of 2 years' duration. He had noticed intermittent gross, painless hematuria for 3 months. He had no other important complaints, and the past history and system review were noncontributory.

Physical examination revealed a somewhat obese man. Blood pressure was 170/100, and a small umbilical hernia was present. No tenderness was elicited over the pubic bone. There were no other abnormal findings. Voided urine on this occasion was grossly bloody. Laboratory studies revealed no other abnormalities.

Cystoscopy revealed no intravesical disease except for several small submucosal hemorrhages around the right ureteral orifice. The right ureter was blocked intramurally to all catheters. A bulb ureterogram was done (fig 1, A) and revealed a narrow segment of the lowermost ureter above which the ureter became dilated. The lowermost portion of the dilated ureter was irregular and contained a small filling defect. Roentgenograms made previously (fig 1, B) showed a considerable right ureterohydronephrosis with no visible ureteral calculus, and an excretory urogram done on May 9, 1949 showed the same findings. The original impression was that the lower ureter was obstructed by a neoplasm, stricture, or nonopaque calculus.

The patient was admitted to Mt Sinai Hospital and on June 6, 1949 the right lower ureter was explored. A dilated ureter was found and was mobilized caudally towards the bladder. The lower ureter below the iliac bifurcation was surrounded by an inflammatory mass and was acutely angulated. A biopsy of the mass was taken and immediate frozen section showed only acute and chronic inflammatory tissue. The ureter was then opened and a large catheter was easily passed into the bladder. Portions of the mucosa were removed for study. These subsequently revealed only acute inflammation. A T tube was placed in the ureter and the wound was closed.

Postoperatively the patient did well. The T tube was removed after 2 weeks after an excretory urogram showed good right-sided visualization. There was, however, no decrease in the degree of the right ureterohydronephrosis. After the T tube was removed, the patient began to leak urine through the wound.

The right kidney was found to weigh 520 gm and measured 13.5 by 8.5 by 6.5 cm in dimensions (fig 3, A). A 7 cm length of ureter was attached to the pelvis. The capsule of the kidney stripped with ease from the lower half of the anterior surface and from the lower pole of the kidney. A large round tumor mass which was found to occupy the upper pole of the kidney measured 8.5 cm in diameter. The cut surface of the tumor showed layers of homogeneous, soft, yellow, fatty tissue separated by zones of dark purplish soft, clotted blood (fig 3, B). The tumor did not appear to involve the anterior half of the kidney, but had merely compressed it downward. The tumor, however, could not be separated from the posterior half of the kidney. The lower pole of the kidney appeared to be spared by the tumor, and a fairly sharp line of demarcation existed between the tumor and the kidney in that region. The tumor bulged into the surrounding perinephric fat and appeared to be grossly fairly well encapsulated in the perinephric region. Microscopically, sections from the tumor revealed adult-type fat cells contained in a reticular, fibrous stroma. The cells were characterized by vacuolated cytoplasm and eccentrically placed flattened basophilic nuclei with prominent nucleoli. In some fields there were large areas of hemorrhage with masses of red blood cells and fibrin apparent. In other areas many small focal hemorrhages were seen and at some points the areas of hemorrhage were surrounded by foci of lymphocytes and plasma cells and scattered polymorphonuclear leukocytes. Proliferating fibroblasts and mononucleated phagocytes, many of which contained golden brown pigment were also present. Multinucleated giant cells were sometimes seen in these areas. Scattered lymphocytes and plasma cells and many congested capillaries were observed throughout the stroma of the tumor. Fat cells of a more immature variety were seen in some fields and displayed granular neutrophilic cytoplasm and large centrally placed basophilic nuclei with prominent nucleoli. The fatty tumor was encapsulated in some places by dense, fibrous tissue and separated into lobules by broad, fibrous trabeculae which penetrated the tumor substance. Sections from the tumor adjacent to the posterior surface of the kidney revealed that no capsule separated the tumor from the kidney substance but masses of fat cells were seen to penetrate the kidney parenchyma pushing between tubules and glomeruli (fig 4). The fat cells were accompanied by strands of proliferating fibroblasts, many thick-walled capillaries and dense foci of lymphocytes and plasma cells.

SUMMARY

A case of large intrarenal lipoma with massive focal hemorrhages is presented. The roentgen examination is of interest in that there was a deformity of the kidney substance in the pyelograms and the large fatty mass was extremely radio-translucent which sign is prominent on all of the roentgenograms. This x-ray characteristic may be of some importance in the preoperative differential diagnosis of intrarenal lipomas.

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ueter was about 560 r Physical factors were 200 kv, 20 ma, 50 cms target skin distance, and Thoraeus filtration (HVL of 2.0 mm Cu) Treatment was completed on June 10, 1950

On May 19, 1950, three weeks after the beginning of x-ray treatment, the patient reported relief from pain for the first time in several years The voided urine became microscopically negative even though all antibiotics and chemotherapeutic drugs had been discontinued

On July 17, 1950 an excretory urogram showed almost a complete subsidence of the right hydronephrosis and on October 21, 1950 the intravenous pyelogram was entirely normal (fig 2)

The patient has remained symptom free and the urine is microscopically negative



FIG 2

DISCUSSION

The etiology of the ureteral lesion was not elucidated The patient was studied from urological, gastro-intestinal, and hematological viewpoints without help from these investigations Biopsy at operation showed nonspecific inflammatory ureteritis and peri-ureteritis with ureteral stricture Operative and chemotherapeutic approaches to the cure of this lesion were without avail As a last resort the use of radiotherapy was decided upon The result was indeed spectacular and gratifying inasmuch as a complete subsidence of the lesion has evidently occurred

That healing may follow the use of radiotherapy for nonspecific inflammatory lesions of the urinary tract is a fact to be stressed It seems strange that we were unable to find any reports in the literature describing this valuable therapeutic technique for lesions of this nature

or the hemiazygos vein. Usually the third and fourth end in the inferior vena cava. The azygos and hemiazygos veins are the continuations of the lumbar azygos veins. These veins when present may receive the upper two (or more) of the lumbar veins. The right lumbar azygos is the usual origin of the vena azygos.

The vena azygos is variable in its origin. It usually springs from the back of the inferior vena cava at the level of the renal veins but may begin between the diaphragm and the body of the 12th thoracic vertebra as the continuation of the right subcostal vein or from the junction of that vein and the right ascending lumbar vein.

Regarding the embryology of these veins Cunningham states: The posterior cardinal, subcardinal and supracardinal veins, the thoraco-lumbar veins, pre-vertebral venous plexuses, azygos venous lines and the inferior vena cava

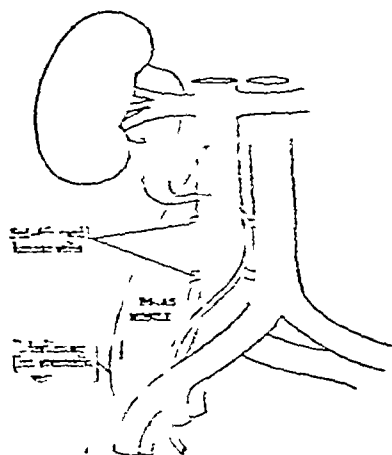


FIG. 1 Showing abnormal course of right ureter as seen at operation

receive in turn as they supplant one another the inter-segmental veins which open first into the posterior cardinals and finally in the thoracic region and in some cases and to a variable extent in the lumbar region into the adult representatives of the azygos venous lines.

The terminations of the lumbar veins and the origin of the azygos vein are thus so variable when the inferior vena cava develops normally that any bizarre arrangement of the tributaries can be expected in the presence of an anomalous vena cava. Likewise the relation of the ureter to these tributaries may be very variable.

Pick and Anson found a postcaval ureter in the course of a routine laboratory dissection and described the venous pattern in detail. The ureter was suspended in a V shaped venous crutch on the posteromedial aspect of the inferior vena cava. The medial limb of the V was a tributary of the vena cava formed by the union of the lumbar azygos vein and the second right lumbar vein. The lateral limb was formed by the vena cava itself. Similarly McElhinney and Dorsey found that the postcaval part of the ureter in their case was caught up on a

September 1946 Admitted for cesarean section Blood urea 54 mg 100 ml

August 1947 Complained of anorexia, nausea and vomiting History of left pyelonephritis 3 months previously Blood urea 53 mg/100 ml Excretory urogram showed staghorn calculus of the left kidney (fig 1, A) with practically no excretion, and on the right side gross hydronephrosis and hydro ureter (fig 1, B)

October 1949 Complaining of loss of weight, and gave history of frequent attacks of right renal colic, sometimes associated with rigors On abdominal examination the right kidney was palpably enlarged and tender Calculus unaltered, no excretion on left, right hydronephrosis and hydro ureter slightly



FIG 1 Case 1 A, staghorn calculus, left kidney B, excretory urogram 90 minutes Gross right hydronephrosis and hydro ureter C, excretory urogram, 20 minutes Considerable improvement in right hydronephrosis Right ureter not apparent in any of the films

increased Blood urea in the interval had been as high as 105 mg 100 ml October 25 Admitted Queen Elizabeth Hospital and after preparation of the colon, operation was performed by Mr Hugh Donovan on October 31 Right pararectal incision The right ureterocolic junction was exposed and the ureter was found to be dilated to about 1 cm in diameter (fig 2) The seromuscular suture line appeared to have given way so that the ureter was only covered by a few fibrous strands The colon was opened by a transverse incision 3 cm in length and the stomach of the ureter was found to be markedly stenosed It would not admit a fine probe The mucosa was slit up proximally for 1 cm (the stricture was found to be confined to the extreme end of the ureter) and ureteric and colic mucosal layers were sutured together for the length of the incision with a few interrupted sutures of fine plain catgut The colon was closed in two layers and the abdomen sutured without drainage Discharged from hospital 19 days later

January 1950 Considerable improvement in the right hydronephrosis and the

and a mild degree of hydronephrosis was present. There was no obvious compression of the ureter by the inferior vena cava. The stone was thought to be the cause of the hydronephrosis and this view was confirmed when an almost normal pyelogram was obtained 8 months after its removal.

Summing up these divergent views it may be said that: 1) The postcaval ureter is not necessarily associated with hydronephrosis. 2) The postcaval ureter may be compressed by the abnormal vena cava or by one of its tributaries. 3) Ptosis of the right kidney may result in a severe ureteric kink over a lumbar tributary of the anomalous vena cava. 4) Prolonged pressure on or kinking of the retrocaval part of the ureter may lead to the development of a stricture. 5) A calculus impacted in the postcaval ureter may be the sole cause of obstruction.

If reparative surgery is contemplated the relative importance of each of these factors as a cause of the hydronephrosis should be assessed.

DIAGNOSIS

A diagnosis of postcaval ureter should be considered in any case of right hydronephrosis of obscure etiology. The diagnosis is established by determining the course of the ureter radiographically. A retrograde catheter may or may not enter the pelvis. The diagnostic criteria have been well established by Randall and Campbell, Harrill and others. They are the following:—

1) On an anteroposterior view the ureter presents a sickle-shaped or S shaped curve reaching towards, to or beyond the midline of the body, the convexity of the lower curve being directed upwards and medially.

2) In an oblique view the ureter impinges on the lower lumbar spine, whereas the normal ureter lies at some distance anterior to it.

3) With a stereoscopic view the radius of curvature of the lower convexity of the ureter should be large enough to enclose a structure having the diameter of the inferior vena cava.

4) The upper fourth or more of the ureter may be dilated on a ureterogram. The lower ureter is undilated.

In view of these well established radiographic features it is difficult to agree with Young, who writes "Preoperative diagnosis is likely to remain a rarity." I believe that a diagnosis could always be made beforehand and treatment planned accordingly.

TREATMENT

A survey of the literature shows that treatment has not been entirely satisfactory. Table I is an analysis of all cases surgically treated to date. Apart from nephrectomy the usual procedure has been to divide the ureter, bringing the two ends in front of the inferior vena cava and anastomosing them over a ureteric splint, performing a nephrostomy at the same time. There have been minor modifications of this technique. McElhinney and Dorsey, and Goyanna excised a constricted portion of ureter. Greene and Kearns left the postcaval segment of the ureter in situ but then had to mobilize the kidney and fix it to the quadratus lumborum muscle at a lower level to relieve tension on the anastomosis.

cated by ligation of both ureters at the pelvic brim and treated by reimplantation of the left ureter in the bladder and right uretero-colic anastomosis by Riches' extraperitoneal method. Convalescence was complicated by the development of an abdominal fistula.

August 1948. Showed gross dilatation of the right pelvis and ureter (fig 3, A).

December 1948. Some decrease in the right hydronephrosis and hydro-ureter but leakage from the abdominal fistula continued. Blood urea 33 mg/100 ml.

January 1949. Operation, Mr Hugh Donovan. Oblique incision in R I F with extraperitoneal exposure of ureterocolic anastomosis which was found to be in an abscess cavity containing a grape pip, and communicating with the colon by

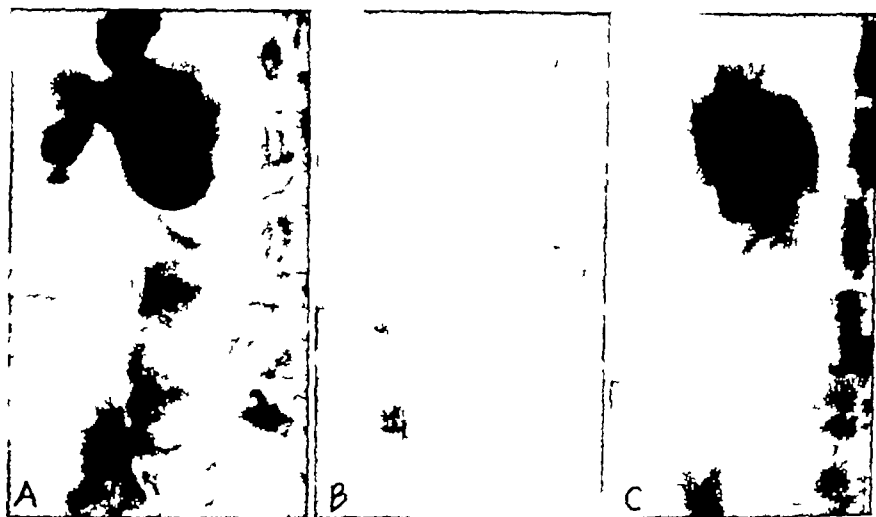


FIG 3 Case 24, excretory urogram 90 minutes. Gross right hydronephrosis and hydro-ureter. B, plain x-ray. Pelvis and ureter of right kidney outlined by gas. C, excretory urogram, 35 minutes. Right hydronephrosis and hydro-ureter still present, but no ureteric hold up, as in previous series of urograms.

a small opening. This opening was enlarged in a longitudinal direction and the ureterocolic junction was found to be markedly strictured, it was slit up and the opening closed in a transverse direction, in the manner of a Mikulicz-Radecki ureteroplasty for hydronephrosis, with two layers of interrupted sutures of 0000 chromic catgut. Uneventful convalescence.

September 1950. Complaints of occasional pain in right loin. General health good and has gained 42 lbs (19.09 kg) in weight since operation. Slight tenderness in right loin. Blood urea 44 mg/100 ml. Straight x-ray of renal tract shows right pelvis and ureter outlined by gas (fig 3, B). Urograms show that the right hydronephrosis and hydro-ureter are still present but there is no ureteric hold up as in the preoperative urograms (fig 3, C).

When examined by urography in November 1951, the improvement in the patient's condition had been maintained.

CONCLUSIONS

The pre-ent methods of preparing the bowel for colonic surgery make stomatotomy a justifiable procedure in view of the progressive nature of the

admits that the method is unduly elaborate but gives no reason for choosing two incisions. Even Uebelhör performed ureteric section and re-anastomosis, although he was certain that the right testicular vein and not the inferior vena cava compressed the ureter in his patient.

Many cases of ureteric section and re-anastomosis were complicated by leakage, infection or stricture formation at the anastomotic site. Nourse and Moody reported postoperative infection and delayed healing of the nephrostomy wound. Following an attempt at repair of the ureter the kidney was removed 5 months later. In the case of Greene and Kearns, there was infection and leakage at the anastomosis. They considered that the leak was due to early removal of the ureteric splint and felt that ureteric dilatation would be necessary later. A postoperative ureterogram in the case of McElhinney and Dorsey suggested a stricture, and ureteric dilatation was recommended. Creevy's case required ureteric dilatation for 3 months and it was feared that a stricture would develop. Shearer was also dogged by stricture formation. A constriction at the ureteropelvic junction in Kimbrough's case required dilatation. Lowsley designed an operation to preserve the neuromuscular mechanism of the ureter and to eliminate stricture formation. He cut the ureter just outside the bladder wall, removed it from behind the inferior vena cava and re-implanted it into the bladder. He had to re-operate after 6 weeks for a ureteric stricture above the site of re-implant. Later, abscess formation with sloughing of the lower end of the ureter necessitated skin ureterostomy because the other kidney was functionless. Creevy attributes this result to impairment of the ureteric blood supply because of the wide mobilization of the ureter in Lowsley's procedure.

Harrill divided the renal pelvis rather than the ureter to avoid the development of a stricture. With the same end in view, Anderson and Hynes devised a ureteropelvic repair. In both these cases a satisfactory result was obtained. Young simply removed a calculus impacted in the retrocaval part of the ureter.

Summarizing the treatment of the 20 cases traced in the literature, primary nephrectomy was done in 6, nephrolithotomy in 1 who died, ureterolithotomy in 1 and ureteric or pelvic section and re-anastomosis in 12. Of these 12 cases, strictures developed in 7, severe enough to demand nephrectomy in one and skin ureterostomy in another. Only 3 had a satisfactory result. Of the remaining 2 cases one was said to have a good result but no pyelograms are shown, no mention of the end result is made in the other case report.

In the case described here, pressure on the ureter was relieved, and the ureter allowed to take up a more normal position by section of the inferior vena cava.

CASE REPORT

C. S. a man aged 40, who was referred by his doctor to a consultant physician, complained of frequency and scalding of micturition and a dull aching pain in the right loin of 7 weeks duration. There was no radiation of the loin pain. Physical examination was negative but a mid-stream specimen of urine contained albumin, pus cells and erythrocytes. B. coli was obtained on culture.

THE RESPONSE OF THE URETER AND PELVIS TO CHANGING URINE FLOWS

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Extensive studies on the physiology of the ureter have been previously conducted. The methods of investigation used in former studies can be divided into three groups: 1) visual inspection of the ureter *in situ*, after laparotomy exposure,^{1, 2} 2) observations made on excised ureteral strips placed in artificial nutrient solutions,^{3, 7} and 3) studies of pressure changes in the ureteral lumen after introduction of a cannula or a catheter into the ureter.^{8, 13} The first two procedures create abnormal conditions, while the third entails the presence of a foreign body in the ureter which may disturb the normal behavior of this organ. Studies of the pelvis have been largely limited to pyeloscopic and pyelographic observations.^{14, 16}

We have investigated the response of the ureter to variations in urine flow in resting, trained, unanesthetized dogs by measurement of urine flow, spurt frequency and spurt volume in animals with exteriorized vesical trigone, and also by kymographic tracing of the urine discharged from the ureters as an index of peristaltic activity. These methods avoid the criticisms that may be leveled against previous observations. Pressure changes in the renal pelvis were also studied during varied urine flows in anesthetized animals.

METHODS

Three female dogs were used: dog 1, weighing 6.5 kg; dog 2, 18 kg; and dog 3, 19 kg. Under sodium pentobarbital anesthesia, the vesical trigone with the adjacent floor of the bladder was exteriorized, producing an artificial ectostrophy of the bladder.^{17, 18} Shortly after operation, the dogs were trained to lie upon

Aided by a grant from The Commonwealth Fund

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¹⁰ Trattner, H. R. *J. Urol.*, **11**, 477, 1924.

¹¹ Trattner, H. R. *J. Urol.*, **28**, 1, 1932.

¹² Ockerblad, F. M., Carlsson, H. I. and Simon, J. F. *J. Urol.*, **33**, 356, 1935.

¹³ Lapides, J. *J. Urol.*, **59**, 501, 1948.

¹⁴ Herbst, W. *J. Urol.*, **26**, 233, 1931.

¹⁵ Jones, J. I. *Proc. Roy. Soc. Med.*, **29**, 263, 1936.

¹⁶ Narath, P. A. *J. Urol.*, **43**, 145, 1940.

¹⁷ Pilecher, F., Bollman, J. I. and Mann, I. C. *J. Urol.*, **38**, 202, 1937.

¹⁸ Maluf, N. S. R. *Ann. Surg.*, **130**, 43, 1949.

¹⁹ Morales, P. A., Crowder, C. H., Jr., Fishman, A. P., Maxwell, M. H. and Gomez, D. M. *Am. J. Physiol.*, **163**, 454, 1950.

was made and the right kidney and ureter were explored through an oblique lumbar incision on April 4, 1949

The general mass of the kidney was normal externally. Palpation of the intact pelvis showed no stone. On exposing and freeing the ureter, it was found to pass behind the inferior vena cava at the level of the third lumbar vertebra. The inferior vena cava was easily separated from the ureter which descended behind its left margin and curved forwards in front of it just above the union of the common iliac veins. The ureter was traced down to the pelvic brim and seen to cross in front of the common iliac vessels in the normal way. Likewise the right testicular vessels bore a normal relationship to the ureter. There was dilatation of the ureter from the ureteropelvic junction down to the point at which it passed behind the inferior vena cava. The lower ureter was undilated.



FIG. 3. Infra red photographs showing well marked superficial venous collateral circulation which had developed 3 weeks after section of inferior vena cava.

The horizontal, retrocaval part of the ureter appeared to be constricted. Active peristalsis was soon evident, however, in the renal pelvis and throughout the entire length of the freed ureter. From this observation it was concluded that the inferior vena cava was compressing the ureter in this case, and after tying off two right lumbar tributaries the inferior vena cava was sectioned between two silk ligatures at the level of the third lumbar vertebra. Marked retraction of the cut ends of the vena cava, especially the upper, was then seen, which confirmed the impression that the inferior vena cava had been under tension in front of the ureter. The retrocaval part of the ureter was now completely free and could be easily replaced to its normal position over the psoas muscle. Redundancy of the freed ureter did not appear to interfere with its function and nephropexy was not considered necessary. The wound was closed in layers with a tube drain.

On the following day the superficial veins of both legs were engorged but there

tion in increasing doses. The changes in pelvic pressure, together with the corresponding urine flows and peristaltic rates were recorded.

RESULTS

Direct observation of peristaltic activity The ureteral orifices were observed to open and close, allowing urine to squirt out intermittently. During low

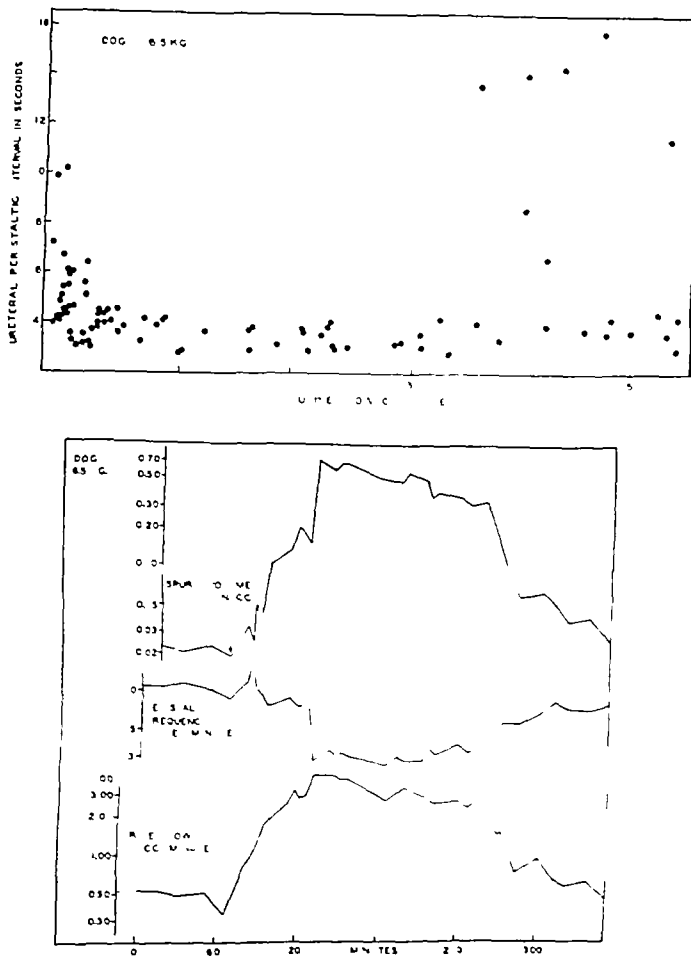


FIG. 1 (Upper) peristaltic interval related to rate of urine flow. At urine flows above 0.5 cc/min peristaltic interval tends to remain constant at 3 to 5 seconds. (Lower) change in urine flow, peristaltic frequency and spurt volume during water diuresis. Note that a marked increase in spurt volume, in the face of decrease in peristaltic frequency, accommodates increased urine flow.

urine flows, the spurts were barely perceptible, issuing weakly from the ureteral openings. As the flow increased, the urine emerged with more vigor. During marked diuresis, the urine spouted out from the ureters to distances of over 30 cm, each jet of urine lasting for several seconds. With extreme osmotic diuresis, the peristaltic nature of the flow disappeared, and instead the urine poured out from the orifices in a continuous stream at lower pressures.

charged from hospital on the twenty-fourth postoperative day, when the right long saphenous vein was still thrombosed and there was some edema of the right thigh

Excretory urograms obtained 3 months after operation show a marked diminution in size of the hydronephrosis (fig 4) There was only slight edema of the right calf and the right long saphenous vein was no longer palpable

Six months after operation the patient had no complaints All edema had disappeared (fig 5) and he had resumed his previous occupation as a motor mechanic The urine was sterile but contained a few red cells Excretory urograms show no change from those obtained at 3 months

DISCUSSION

As in any case of hydronephrosis, a decision has first to be made whether the kidney can be saved Undoubtedly nephrectomy is the most rapid and certain method of relief and should be done when reparative surgery is contra-indicated

Apart from nephrectomy, attention in the past has been focused on the ureter In some cases, however, the abnormal inferior vena cava has been shown to compress the underlying ureter, which has been otherwise normal Thus, pressure on the ureter may be the sole cause of the hydronephrosis and in such a case it seems rational to relieve it, provided no ill effects follow

Sufficient evidence has accumulated in recent years to show that ligation of the inferior vena cava below the level of the renal veins is a safe, benign procedure, free from undesirable sequelae in the majority of cases (Hyman and Leiter) The inferior vena cava has been ligated mainly for extensive deep vein thrombosis or septic thrombophlebitis complicated by pulmonary embolism Many authors remark on the absence or transient nature of the postoperative edema When present, it seldom incapacitates the patient (Gaston and Folsom, Moses, O'Neil) Ray and Burch, after a careful clinical and physiological study of 12 cases of ligation of the inferior vena cava for pelvic thrombophlebitis, detected no detrimental effects There was no diminution in functional capacity, general or local All the patients were able to do their usual duties These writers concluded that the circulatory adjustments following ligation of the inferior vena cava were adequate although not fully understood In the light of these findings even less disturbance of function can be anticipated when the inferior vena cava is ligated in the absence of deep vein thrombosis

While section of the inferior vena cava may seem a drastic procedure, it should be remembered that in several cases the infra-renal vena cava was bilateral, only the right ureter being postcaval (Harrill, Uebelhör, Rotter, 1 case each, Adachi 2 cases) In others the right ureter was found to pass between two right inferior venae cavae (Wicke, Rotter, Gierke) In other words, the abnormally-placed inferior vena cava may not always drain as wide a field as the normal vein In such circumstances it could no doubt be sectioned with impunity Preoperative information on the venous pattern might be obtained by venography in any case the arrangement of the veins can be ascertained at operation The double vena cava on the right side should be easily seen When

a marked diuresis of about 11 cc/min, the frequency of peristalsis decreased to about 2 per minute. It will also be noted that the increase in the amplitude of the waves paralleled increased urine flows. The tracings of peristaltic frequency were continuously checked against direct observation, for without this precaution, interpretation would have been difficult because of numerous artefacts (*vide infra*).

Manometric study of pelvic pressures Figure 3 illustrates the relation of pelvic pressure to urine flow. The pressure within the renal pelvis increased with increasing urine flow until conditions of extreme diuresis were reached, when further increases in the urine flow were no longer accompanied by corresponding increases in pelvic pressure. It was consistently observed as before, that during extreme diuresis the urine poured out of the ureters in a continuous stream.

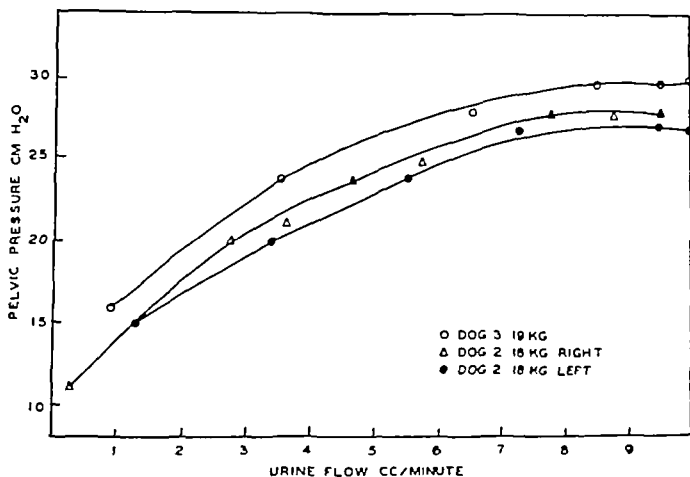


FIG 3 Pelvic pressure in relation to urine flow

The frequency of ureteral peristalsis during these experiments conformed to our previous observations. No alteration in the peristaltic frequency was observed when pelvic pressure was artificially increased by gradually elevating the manometer, or increasing the height of the water column. At very low urine flows, no positive pelvic pressure could be recorded in the manometer. During moderate diuresis, the pelvic pressure averaged 10 to 15 cm water.

Pulsations were observed in the fluid column of the pelvic manometer, which were however indistinguishable from those due to respiratory movements. During increased urine flows, the pulsations fluctuated to as much as 7 cm in the column, but there was no way of determining whether their movements were attributable to peristaltic inflow of pelvic urine into the ureter or to active contraction of the pelvic musculature.

DISCUSSION

Most investigators have held the opinion that urine pressure, by distention of the ureteral wall, initiates and influences the peristaltic activity of the

In conclusion I must record my gratitude to Mr Hugh Donovan whose fertility of ideas has been a source of inspiration in writing this paper

Since this paper was submitted for publication several cases have been added to the literature, confirming the opinion advanced above that the incidence of retrocaval ureter is higher than previously supposed

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length. Thus in the pelvis and ureters, distention due to increased urine pressure during diuresis stretches the smooth muscle and causes more powerful contractions.

Others have presented evidence that the rhythmic contractions of the ureter are entirely independent of extrinsic nervous influences.¹³⁻²² The smooth muscle of the ureter, like cardiac muscle, exhibits automatic rhythmicity and therefore can initiate muscular contractions without the necessity of external neural connections. Excised strips of ureter are known to give spontaneous rhythmic contractions.^{1, 3, 4, 6, 23} Studies on the relative activity of various segments of the excised ureter of the dog²² have shown that the pelvic third exhibited the greatest degree of rhythmicity, and the vesical third, the least. These observations recall the frog's heart, where separate recordings of the contractions of each of different parts reveal a descending scale of rhythm from the sinus to the bulbus, contraction of the sinus being the most frequent.²⁰ In the heart, the portion with the greatest rhythmicity imposes its rhythm on the other structures, and is called the pacemaker. Bozler²¹ in a study of action potentials has shown that the rhythmic waves of contraction which sweep over the ureter start in a restricted area at its extreme renal end and refers to this zone as the 'pacemaker' of the ureter.

The pyelographic and pyeloscopic studies cited earlier have shown that not only the ureters, but also the pelvis and its calyces exhibit rhythmic peristaltic activity. The calyces contract in succession from above downwards. As soon as the superior calyx contracts, the sphincter at its neck relaxes, permitting the calyceal content to be expelled with varying degrees of completeness into the pelvis. At the completion of this contraction, the sphincter contracts, preventing regurgitation from the pelvis into calyces. The lower calyces then contract in turn. As the lower-most calyx delivers its contents, the pelvis contracts, propelling its contents into the ureters, and initiating a peristaltic wave which is propagated along the ureter.

Since peristaltic contractions occur in the calyces, it is possible that the pacemaker resides in a supra-ureteral structure, rather than in the extreme renal end of the ureter, as postulated by Bozler. The maintenance of a limited range of peristaltic frequency despite variations in urine flow during moderate diuresis conforms to these views.

The observed decrease in peristaltic frequency with very low urine flow can be ascribed to limitations in our method of direct observation. It is probable that some peristaltic contractions could have been missed because there was no accompanying urine to form a 'spurt'. Evidences indicate that the intact ureter continues contracting rhythmically despite the absence of urine.^{2, 11}

The capacity of the ureter to adapt itself to changes in urine volume is limited

² Davalos, A. *J Urol* 58: 22, 1947.

¹⁰ Starling, E. H. *Principles of Human Physiology*. Philadelphia: Lea & Febiger, 4th ed. 1926.

²¹ Bozler, F. *Am J Physiol* 136: 543, 1942.

²² Fowler, H. A. *Trans Am Assoc Gen Urin Surg*, 5: 35, 1910.

²³ Graves, R. C. and Davidoff, L. M. *J Urol*, 10: 185, 1923.

Cystoscopy was done again and on this occasion the right ureter was obstructed at 5 cm. The patient was discharged on June 22, 1949 to await spontaneous healing of the ureteral fistula.

The fistula continued to drain until July 20, 1949 and then became dry. An excretory urogram at this time showed the considerable right ureterohydronephrosis as previously. The patient still complained of right pubic pain, and the voided urine contained many white blood cells and red blood cells microscopically. In spite of the administration of a variety of antibiotics and cystoscopic dilatation of the right ureter on November 17, 1949 and January 12,

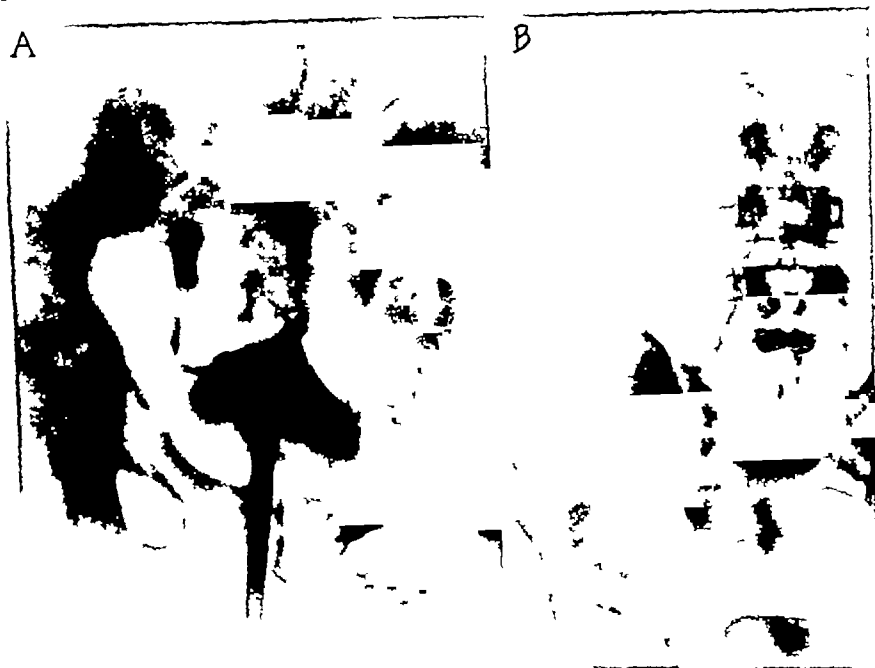


FIG 1

1950, pain and pyuria persisted. Barium enema, sternal marrow aspiration, and studies of the urine for acid fast organisms were all without positive results. X-ray studies continued to show an advanced right ureterohydronephrosis.

On April 24, 1950 cystoscopy was repeated. On this examination there was an area of inflammatory reaction and bullous edema surrounding the right ureteral orifice. Biopsy of this tissue showed vascular bladder mucosa. There was no evidence of tumor.

Because of the apparent failure of all the methods used, it was decided to treat this apparently nonspecific granulomatous inflammatory lesion with small doses of radiotherapy directed to the lower end of the right ureter. Consequently, the first treatment was given on April 28, 1950 in the hospital and continued thereafter on an ambulant basis. A series of 12 treatments was given. The x-rays were directed to the lowermost position of the right ureter from anterior and posterior portals, each field receiving 600 r (mr) in a period of 6 weeks. The anterior field size was 10 by 15 cm, while the posterior was 15 by 20 cm. The estimated tissue dose in the region of the juxta-vesical portion of the right

TRANSILLUMINATION OF THE BLADDER A PRELIMINARY NOTE

DIOMEDE PETILLO

The object of this note is to introduce transillumination of the bladder cavity, by rectum or by vagina, as a possible adjunct to, and a useful accessory for, cystoscopic examination

Its aim is two-fold 1) to visualize, by transparency, features and lesions that are beyond the optical possibilities of the cystoscope and it would be accomplished by looking into the distended bladder through a blind (no light) cystoscope while the vaginal or rectal light-carriers are in operation (transillumination proper), 2) to add clarity, brilliancy and precision to the cystoscopic vision by utilizing both sources of light, the cystoscopic and the retrovesical, in unison

It is true that the range of action of transillumination is, for obvious anatomical reasons, restricted to a segment of the bladder trigone, paratrigoal areas, ureteral meati, vesical neck, prostate gland and, to some extent, fundus and lateral walls, but it is equally true that it is just this segment where the most important and most common lesions are met and cystoscopic exploration exercised

To be sure, a transillumination worthy of the name should give us a reasonable amount of information on the gross anatomic texture of the bladder wall so that, once established what the picture of a normal wall looks like, we should be able to tell whether, in a given case, any more or less abnormal change has taken place in its thickness This would be particularly helpful in cases of tumors

If in other words, we could prove the presence of a constant positive opacity at the basis of malignant tumors as an index of deep infiltration in contrast with a negative opacity at the basis of benign ones, we would be in possession of a very useful tool in the differential diagnosis, probably more reliable, indeed, than biopsy itself Whether all this can be attained in clear-cut terms is, of course, another story, one would feel, however, that if the degrees of opacity obtainable were to offer only criteria of probability, transillumination may prove not to have been tried in vain

Likewise zones of abnormal opacity in the field of the prostate gland should help to put the examiner on the alert for possible malignancy or prostatic calciosis The same way stones impacted into the intramural portion of the ureter could be easily detected and, perhaps, the measure of fibrotic degeneration of the neck more clearly defined and one may be allowed to suspect that even the resectionist could find some advantage and some comfort in transilluminating his field of action

As to the other aspect of transillumination regarding the over-intensification of light no one, I surmise, can argue about its desirability Diverticula pinpoint ureteral meati, new growths, urinary incrustation, chronic inflammations

OPERATIVE PROCEDURES FOR STENOSIS FOLLOWING URETEROSIGMOIDOSTOMY

D ST CLAIR L HENDERSON

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The late results of ureterosigmoidostomy are not infrequently unsatisfactory due to the occurrence of stricturing of the terminal ureter. Higgins (1937) showed that hydronephrosis and hydro-ureter were not associated with intra-rectal pressure or incompetence of the valvular mechanism, and discussed the incidence of stricture in animals and patients following operation. More recently, Nesbit (1949) has noted that this may occur where the ureter enters the bowel due to tight suturing of the bowel serosa, in the tunnel, or at the ureteric opening, and has devised his direct elliptical connection to the colon to prevent its occurrence.

The presence of a stricture is indicated by progressive hydronephrosis, with or without calculus formation and hydro-ureter, which, depending on the condition of the other kidney, may be associated with diminution of the renal function, as shown by the blood urea, and untreated, progress to complete loss of function on the affected side, and finally nephrectomy may be necessary.

Follow-up by excretory urography at yearly intervals, or more frequently if hydronephrosis has been noted, will detect the presence of the condition and permit treatment before damage to the kidney is too gross.

The possible lines of treatment are 1) nephrostomy, 2) cutaneous ureterostomy, 3) division of the ureter proximal to the anastomosis and re-implantation in the colon, which is, of course, associated with the possibility of its recurrence, 4) performance of a plastic operation on the stricture "stomatotomy." The object of this paper is to describe the operative procedures carried out in 2 cases. It is appreciated that the follow-up period is short, but the importance of the condition merits a preliminary report.

CASE REPORTS

Case 1 B. T., aged 30 years

January 1943 Transplantation of ureters for an extensive vesicovaginal fistula following obstructed labor. Preoperatively there was slight bilateral hydronephrosis and hydro-ureter, and prior to discharge from hospital the hydronephrosis on the right was slightly greater.

November 1944 Definite hydronephrosis with considerable dilatation of the right ureter, normal left urogram. Complaining of pain in the right loin.

April 1946 Patient pregnant and complaining of pain in both loins, worse on the left. Excretory urogram showed no change.

August 1946 Admitted to hospital with pnelitis of pregnancy. Physical signs confined to the left kidney. Condition responded to sulfamezathine and penicillin. Discharged from hospital after 12 days. Excretory urograms showed a staghorn calculus of the left kidney with diminution of function and marked right hydronephrosis and hydro-ureter.

THE URINARY TRACT AS A CAUSE OF DEATH IN PARAPLEGIA

KNOWLTON E BARBER AND ROLAND R CROSS, JR

It has now been 6 years since the end of the war and approximately $4\frac{1}{2}$ years since the Veterans Administration took over the care of the paraplegics at Vaughan General Hospital. Sufficient time has elapsed to warrant a study of the delayed causes of death among the paraplegics, in order to ascertain whether the patients are dying of causes other than those which followed World War I or if they are dying of the same cause but at a slower rate. According to Kennedy,¹ following World War I, 80 per cent of the paraplegics were dead within a few weeks as a result of either urinary infection or decubitus ulcers or a combination of both. Thomson-Walker² estimated that in Britain after World War I 80 per cent of the patients died of urinary infection. Kuhn³ stated that only 20 per cent of patients with spinal cord injury in World War I were successfully evacuated to the United States, and of these, only 10 per cent survived the first year.

During the interval between World War I and World War II, the number of paraplegics at any one location was never very large. Thus, the problem of caring for them was never attacked with any degree of strength except by few men. As a result of World War II and its accompanying large number of casualties renewed interest in the care of the paraplegic was again manifested. Certain progress had been made in the care of the paraplegic between the two wars, and certain alterations in treatment have been made. Following World War I, it was the rule, for a period of time, not to insert any catheter into the bladder but rather to let the bladder overflow. It was believed that this would reduce urinary infection which the catheter carried into the bladder. In World War II this was changed so that, for purposes of ease of transportation and, also, to prevent overdistention, most cases were evacuated from the battlefields with a suprapubic cystostomy. Furthermore, during World War II, the initial spinal cord lesion was in many cases attacked definitively by neurosurgeons in forward units. A third improvement in World War II was the availability of whole blood along with the sulfa drugs and penicillin. These factors resulted in a much larger number of paraplegics being returned to the United States. To take care of them, paraplegic centers were established. In these centers, the personnel and equipment were organized to take care of the specific problems of the paraplegic. This resulted in teams of neurosurgeons, neurologists, plastic surgeons and urologists all being available for their care.

Much has been written in the latter years of the war and since the war in regard to the reestablishment of the paraplegic so that he could take a more active interest in society. The resulting impression has been that with present day methods of treatment the paraplegic has an excellent outlook for life and for the enjoyment of life.

¹ Kennedy, F. *Ann Surg* 24: 1057, 1946.

² Riches, I. W. *Brit J Surg* 31: 135-146, 1943.

³ Kuhn, O. O. *J Neurosurgery* 4: 40-69, 1947.

ureter is not apparent in any of the series Blood urea 82 mg /100 ml (fig 1, C)

July 1950 Improvement in x-ray appearance maintained

The patient was re-admitted in view of persistent left loin pain in November 1950 Her blood urea was then 94 mg /100 ml, hemoglobin 56 per cent The left

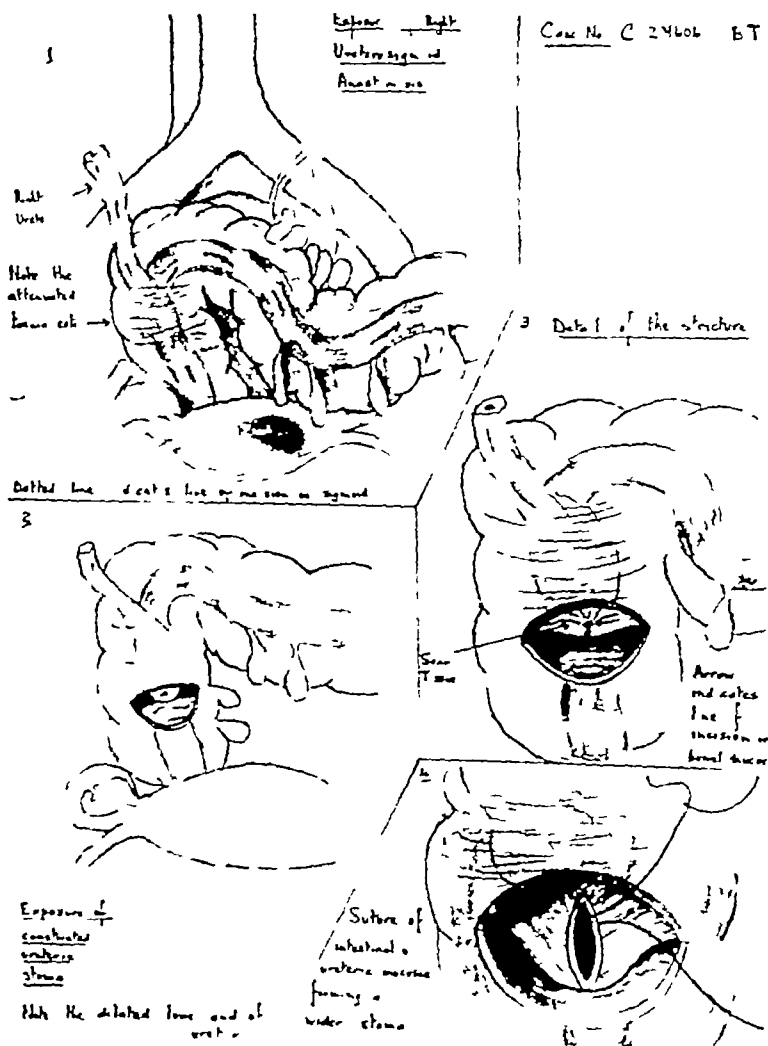


FIG. 2. Case 1. Details of operation on strictured ureterocolic stoma.

kidney was explored November 18, 1950, and nephrolithotomy followed by nephrostomy was carried out. Following operation the blood urea rose, and the patient eventually died on December 27, 1950. Post-mortem examination showed extensive pyelonephritis of both kidneys. The stoma on the operated side (right) was patent.

Case 2. M. J. aged 58 years.

June 1948. Total hysterectomy and bilateral salpingo-oophorectomy compli-

to urinary tract infection and one due to severe decubitus ulcers. Poerl in reviewing 77 cases approximately fifteen months after the war had 1 death, and this was due to a combination of pyelonephritis and pulmonary abscess.

We have divided our paraplegics into two groups: the traumatic group and the nontraumatic group. Among the traumatic paraplegics, of which there are 361, nineteen died, 5.2 per cent. The average duration of life for these 19 patients was 34.9 months. The shortest duration of life was 4 months, and the longest duration of life was 68 months.

An analysis of the causes of death among the 19 cases of traumatic paraplegia indicates that the largest number (11 cases) died of uremia, 57.8 per cent. One patient died of pyelonephritis and mesenteric thrombosis. It was felt at autopsy that the mesenteric thrombosis was really a result of the terminal state, but inasmuch as the blood chemistry determination was not obtained, it cannot be accurately stated that the patient died of uremia although the autopsy findings revealed a definite bilateral pyelonephritis. Two patients died as a result of automobile accidents while they were driving their specially-equipped automobiles. One patient died of ascending myelitis, one died of acute hepatocellular damage, one died of ulcerative colitis, one died of heart failure, and one died of meningitis. If the two who died due to an accident, completely unassociated with any abnormality other than the fact that they were driving a paraplegic-equipped automobile, are excluded, then the result is a death rate of 64.7 per cent of the traumatic paraplegics due to uremia.

Among our cases, there were 145 cases of nontraumatic paraplegia. Among these there are 17 deaths, 11.8 per cent. The average duration of life for these seventeen was 28.3 months. The shortest duration of life was 3 months, and the longest duration was 120 months.

As is quite obvious, in cases of paraplegia due to tumor either primary or metastatic, the patients usually die due to the tumor. An analysis of the cause of death among the 17 cases of nontraumatic paraplegia showed that four of the seventeen had primary tumors of the nervous system, and all four died essentially due to the tumor although in 2 cases it was complicated by meningitis in one and pyelonephritis in the other. Eight cases were paraplegics as a result of metastatic tumor, and all eight died primarily due to the metastatic tumor although one died with additional complications of uremia. This latter case at autopsy showed an obstruction of the lower ureter due to tumor and obviously explained the uremia. One case was due to a brain abscess and died as a result of the brain abscess. In 4 cases a diagnosis was not made as to the cause of the paraplegic state prior to death, and even after death, one was still unexplained. Of the three remaining, one died of a cerebral vascular accident, one of a lung abscess, and one died of an ascending myelitis.

None of these patients had a suprapubic cystotomy for any duration of time during their paraplegic state. This is due to the fact that the medical neurologists feel a suprapubic cystotomy interrupts the fibers of the detrusor muscle and thus interferes to some extent with the physiological functioning of that muscle.

Of the 36 patients who died, only twenty-five had any record of urine cultures.

renal damage, and in the event of its failure nephrostomy or cutaneous ureterostomy may still be carried out

In case 2 the operative procedure has allowed gas from the intestine to pass freely up the ureter and this may be related to the lack of improvement in the hydronephrosis and hydro-ureter compared with the result in case 1 where the condition was of much longer duration

The method adopted in case 2 was necessitated as a result of the local conditions found at operation and appears to be less satisfactory but in both the strictures have been relieved (indicated by free passage of medium into the bowel) It is admitted that the follow-up periods are short, 11 months and 1 year 9 months respectively

In the event of stricturing occurring after Nesbit's operation, the procedure adopted in case 1 would probably still be possible, as although there is no tunnel, the ureter and colon have oblique relations and the dilated ureter could be approximated to the colon proximal to the stoma

SUMMARY

Attention is drawn to the occurrence of stricture of ureterocolic stomata with consequent progressive hydronephrosis and two operations for its relief are described with reports of successful cases The follow-up periods are short

I wish to thank Mr Hugh Donovan, who devised and performed the operations, for permission to report them and Mr A J McG Cathie for permission to reproduce his drawings

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usually responded to treatment. He was injured in November 1943, and got along fairly well most of the time as an automatic bladder. During the course of 45 months of his paraplegic state, he had had many episodes of decubitus ulcers. It was very difficult to keep his blood proteins at anywhere near normal level. In June 1946, a year before his death, his blood protein was 4.1 with albumin of 1.0 and globulin of 3.1. At that same time, the nonprotein nitrogen was 31. He had several attacks of pyelonephritis with chills and fever. Urinalysis showed severe albuminuria on many occasions. The nonprotein nitrogen slowly rose, and on August 20, 1947, it was 90. The patient died 2 days later in severe uremia. No autopsy was obtained. As can be seen, the case was complicated by a severe loss of protein through both the kidney and decubitus ulcers.

Case 3 C B was injured in October 1946. He had a hemothorax, which later required decortication. Later, he had many abscesses of the left kidney. At the time of the pyelolithotomy, severe bleeding was encountered, which required a left nephrectomy in August 1947. After this, increasing ankle edema developed. During his paraplegic state, he had an indwelling urethral catheter. In December 1947, his nonprotein nitrogen was 30, but in January 1948, it was 99. He had convulsions and diarrhea. He died in February 1948, after 16 months of paraplegia. At autopsy examination, the right kidney was very large and pale. The cut section was also very pale. The renal markings were very indistinct. Microscopically, the glomeruli were reduced in number. There was evidence of early glomerular capsule crescent formation. Most of the tubules were dilated.

Case 4 I C was injured in May 1945. Right renal calculi were removed in April 1947. During the first 30 months of his paraplegic state, he had a suprapubic cystostomy. This was allowed to close, and he then had an indwelling urethral catheter. He had many severe decubiti, one of which developed into osteomyelitis of the left femur. He had bladder stones on several occasions and one occasion had a peri-urethral abscess. In October 1947, nonprotein nitrogen was 41, but in April 1948, it was 118. He died 35 months from the time of his injury. At the autopsy examination, amyloid infiltration of both kidneys was found. In addition, the entire right renal parenchyma was one large abscess. There were many small abscesses in the left kidney parenchyma.

Case 5 C H had been a paraplegic for over three years. Most of that time, his bladder was drained by means of an indwelling urethral catheter. After several months, he had some return of function in the left side. On February 15, 1949, he rapidly became dyspneic and cyanotic. Chest x-rays revealed a pleural effusion. The nonprotein nitrogen was elevated for several months, and in fact, in October 1947, about sixteen months previously, it was 75. At the time of the pleural effusion, the nonprotein nitrogen was 125. Oliguria developed and the patient became comatose. He died on February 23, 1949. No autopsy was obtainable.

Case 6 H J was wounded in April 1945 and suffered severe wounds of the arm, back, and chest. A lung abscess and empyema developed. He underwent suprapubic cystostomy. A right renal calculus was removed in April 1947. A rhizotomy was done because of severe spasms. A right lower thigh amputation was done in January 1947, because of osteomyelitis and decubitus ulcers. In

their backs on an animal board with very little restraint. The initial experiments were started 10 days postoperatively.

Direct observation of ureteral peristaltic activity. The ureteral orifices were observed with the naked eye or with the aid of a magnifying glass, the magnitude and frequency of the spurts of urine being carefully recorded.* Ureteral peristaltic intervals were determined by timing with a stop-watch from the onset of one urine spurt to the beginning of the succeeding one, the datum recorded representing the average value of 6 such determinations. The corresponding rates of urine flow were measured by applying to the exposed bladder a suction cup device^{15, 16} which drained the urine coming from both ureteral orifices into a collecting tube. Antidiuresis was induced by water deprivation, and diuresis by oral administration of water or intravenous injection of 25 per cent mannitol solution.

Graphic recording of ureteral contractions. A modification of Trattner's original ureterometric apparatus¹⁰ was used. However, instead of having a catheter in the ureter, a special suction cup was devised and applied to the bladder mucosa. This consisted of a cup having a diameter sufficient to enclose both ureteral openings and which was connected to a suction pump. Within this cup was a smaller bell which just fitted around one of the ureteral orifices and was connected directly to the ureterometric apparatus. Thus when suction was applied, the force of suction was limited to the area within the outer cup but not within the smaller one. This served to hold the cup in place over the bladder mucosa, at the same time it drained out the urine coming from the ureteral orifice lying outside the inner bell. Urine from the other side emptied into the inner bell and the force of its ejection from the ureter was transmitted to the water tambour of the apparatus and recorded as a wave on a moving drum. The concurrent urine flow could be determined by collecting the urine issuing from the needle outlet of the apparatus into a graduated cylinder. This method afforded direct recording of peristaltic frequency and a qualitative index of the force of each peristaltic wave.

Manometric study of pelvic pressures. Using the same animals, the kidney was exposed through a lumbar incision after intravenous injection of sodium pentobarbital. Plastic tubing was threaded through a No. 18 infusion needle which was then cautiously inserted from the convex surface of the kidney into the pelvis; a sudden loss of resistance indicating that the pelvic space had been penetrated. The needle was then withdrawn and the plastic tubing connected to an I-shaped water manometer having a lumen of 1 mm. The pressure within the kidney pelvis was recorded from the manometer after adjusting its zero reading to the level of the pelvis.

To minimize the duration of the experiment, different degrees of diuresis were induced by repeated intravenous injections of 25 per cent mannitol solu-

It was assumed that each spurt of urine represented a peristaltic wave. In several experiments a glass cannula was inserted a short distance into the lower third of the ureter immediately following a spurt of urine, and in all instances the ureter had been completely emptied, no further urine appearing until the next spurt. This confirmed the assumption above.

cept for frequent attacks of chills and fever associated with increased number of white blood cells in the urine. These were diagnosed as attacks of pyelonephritis. He had no renal calculi development, but he did have four episodes of bladder calculi which were removed by lithotripsy. Initially, he had a suprapubic cystotomy, but this was allowed to close after 6 months. For the following 12 months, the bladder was drained by means of an indwelling urethral catheter. With training, an automatic bladder was developed for the 37 months prior to death. What seemed to be bronchitis developed and a chest x-ray was taken in March 1949. The X-ray Department interpreted the picture as revealing a state of uremia. A check of the nonprotein nitrogen revealed it to be 93. The patient slowly became worse and died in March 1949. At the autopsy examination, both kidneys together weighed only 130 gm. They were very tiny. The capsule was stripped from the renal parenchyma with difficulty. Microscopic examination showed some areas of complete fibrosis in between other areas of normal glomerular structure. All the tubules seen were dilated.

As you can see, most of these cases were complicated. The patients did not just die of simple pyelonephritis and uremia. These were cases in which there were repeated physical insults, and evidently, the patient was unable to combat them any longer.

In taking care of paraplegics, treatment must be individualized. A patient who today has an automatic bladder may well be found to have slipped back to a state of having a high residual urine tomorrow. Once an automatic bladder has been established, it does not mean that the condition will remain so. The following 3 cases reveal the care that must be used.

Case 1 H. H., a 33 year old white man, was injured in July 1944. He had a partial lesion of L-1. He had a laminectomy in 1945. For the most part, this patient got along well. He learned watch making and could take care of himself. An automatic bladder developed that was very satisfactory to the patient. However, he did have frequent episodes of a very low-grade fever. As can be seen from figure 1, A, an excretory urogram in March 1949, showed a nonfunctioning right kidney and hydronephrosis of the left kidney. In spite of the patient's opposition, he was replaced on catheter drainage. As can be shown by figure 1, B, in 9 months he had a return of function to the right kidney while the left kidney appeared almost normal. Along with this, his episodes of low-grade fever disappeared almost entirely. This case represented one in which the patient had developed an automatic bladder that was very satisfactory to him. For all practical purposes, it met the requirements of an automatic bladder except that the patient had occasional episodes of fever and the excretory urogram revealed the presence of hydronephrosis. This indicated that the patient was not receiving adequate bladder drainage. Therefore, an indwelling urethral catheter was used to acquire adequate drainage.

Case 2 J. B., a 29 year old white man, was injured in January 1945. For 3 months he had a suprapubic cystotomy. Most of the time following that, the bladder was drained by means of an indwelling urethral catheter. The formation of sacral and ischial decubiti were frequent. The right leg was finally amputated.

Accumulated data of several experiments on one animal relating urine flow to the time interval between each peristalsis are shown in figure 1, *A*. As the flow increased to 0.5 cc/min the interval diminished from 10 seconds to a range of 3 to 5 seconds. Thereafter in spite of further increases in the flow, this interval remained fairly constant until a flow of 4 cc/min was reached. Beyond this the ureteral peristaltic interval became irregularly longer, lasting as long as 17 seconds. The same general pattern was preserved in all the three dogs. However, the peristaltic intervals were relatively longer in the larger animals.

Figure 1, *B* illustrates the interrelationships of urine flow, peristaltic frequency and the calculated volume of each peristaltic spurt of urine during a complete

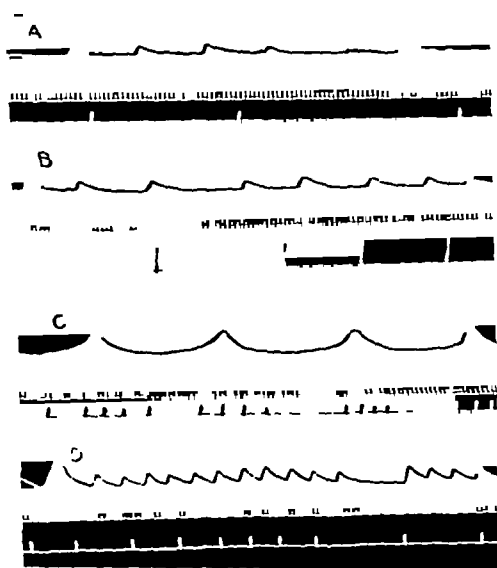


FIG. 2. *A*, *B*, and *C* show (upper line) kymographic tracings of urine discharge from ureters at different rates of urine flow quantities of 1 cc (bottom line). Middle line records intervals of one second. *D* shows false peristaltic curves arising as mechanical artifacts.

experiment on water diuresis. It will be noted that as the urine flow rapidly increased to 4.5 cc/min the frequency of peristalsis slowed from about 10 to 12 contractions per minute to 3 to 4 contractions per minute, where it remained constant despite further increases in the urine flow. On the other hand, the spurt volume increased directly with the increase in urine flow. During the descending phase of the diuresis the spurt volume correspondingly decreased, and the peristaltic frequency increased to control values as normal flow was re-established.

Graphic recording of ureteral contractions. Kymographic tracings obtained from the three animals during different urine flows confirm our direct observations. Figure 2 demonstrates the types of peristaltic waves occurring during different rates of urine flow. In figure 2 *A* the urine flow was 1.5 cc/min and the rate of peristalsis 4 per minute; in figure 2 *B*, the flow was 3 cc/min and the peristaltic frequency was similarly 4 per minute; and in figure 2 *C*, during

removed in November 1949. On two occasions in December 1949, the residual urine was checked and found to be zero on both occasions. Acute epididymitis developed on the right, and rapidly became an epididymo-orchitis which required an orchiectomy. Concomitant with the epididymitis, urinary retention ensued and required drainage by an indwelling catheter. Although the orchiectomy was done about two months ago and all signs of inflammation have subsided, the patient still has not been able to urinate well without the catheter. This is an excellent example of the changes and fluctuations in these patients. They need to be checked at regular intervals because urinary retention may so slowly develop and an elevated nonprotein nitrogen that they may adjust to it. If they are not checked, an irreversible elevated nonprotein nitrogen may develop. This case, also, shows how these patients, even in a good automatic bladder status, may be set back by a genito-urinary infection, the development of a decubitus ulcer, or anything that upsets their general physical well being. Even at the present time, the patient has not been retrained to empty his bladder automatically.

Many patients in whom an automatic bladder develops lose that automaticity by the onset of decubitus ulcers, pyelonephritis, epididymitis, or anything that depletes part of their general physical reserve. Frequently, they may overcome the particular inciting illness but not recover their automatic bladder.

CONCLUSIONS

As can be seen from the foregoing analysis, the main cause of death among the paraplegics is still uremia accompanied by urinary tract infection. The death rate is much lower than after World War I. Much has been done for the paraplegic in relieving decubitus ulcers by means of plastic surgery. Much work has been done in instituting bladder training so that these patients may be able to return to a more active social environment. Bladder training is excellent as is anything else that can be done for the paraplegic to rehabilitate him, but it must not be lost sight of that the kidneys are essential to life. The bladder is a definite social convenience, but the kidneys are essential for living. In taking care of paraplegics, one must ever be alert. These patients may be trained and in good physical condition so that they can return to some form of social and economic activity, but they are still not normal and must be followed. Periodic examinations must be done in order to detect complications during their early stages when they are just developing. Examination of the urine and x-rays of the urinary tract must be done at regular intervals. Preventive medicine must be practiced on these patients. Each time they have decubitus ulcers, pyelonephritis, epididymitis, or any other illness, it is a physical insult on an individual who does not have the reserve. Such insults must be prevented by careful periodic examination.

ureter. According to this concept an increase in urine excretion is accompanied not only by an increase in the amplitude of ureteral contraction but also the frequency of peristalsis.

Lapides,¹² in an extensive investigation of various drugs on the ureter, ascribed the alterations in peristaltic activity recorded kymographically to accompanying changes in urine flow. However, no study of the ureteral response to varying urine volume *per se* (without an accompanying drug) was made. Although he stated that 'an increase in urine excretion will result in an increase in ureteral peristalsis, within limits', he reported no constant changes in the amplitude and frequency of ureteral contractions with increasing urine flow. The objections which may be raised to this method of study are 1) that an indwelling ureteral catheter was used which might act as a foreign body and 2) that the actuality of the recorded peristaltic waves were not verified by direct observation or any other means.

It appears from our observations that the ureters respond to increased urine flow with increased vigor of peristaltic contraction and not by increased frequency, i.e., each peristaltic wave expels a larger volume of urine. The rate of peristalsis remains fairly constant under conditions of moderate diuresis, apparently decreasing at very low or very high urine flows. Intrapelvic pressure increases with urine flow up to marked osmotic diuresis, when it remains at its upper limits despite further increases in diuresis. Artificial elevation of pelvic pressure is not accompanied by any increase in the rate of ureteral peristalsis.

With an apparatus similar to that used by Lapides, but without a catheter in the ureter we attempted to record ureteral peristalsis kymographically. Although most of the tracings obtained corresponded to our direct observations, artefacts were frequently observed. For example, in figure 2, *D*, during an osmotic diuresis the peristaltic frequency as recorded in the tracing was found to be greater than that determined by direct observations made immediately afterwards by a ratio of 3:1. Thus the kymographic record may give an erroneous picture of increased peristaltic frequency with diuresis. These and other artefacts are inherent to the recording apparatus itself, where such factors as resistance in the outflow needle and elasticity of the rubber tambour can cause false intermittency. We believe, therefore that direct visual observation is the preferable way of studying ureteral activity.

The increased vigor of ureteral contraction as the flow of urine is increased is explicable on the basis of known physiological properties of smooth muscle present in the pelvis and ureters. In smooth muscle, as in voluntary muscle, the force of contraction is dependent within physiological limits, upon its

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in one stage and the trigone was then transplanted to this cecal pouch in a second stage. Werelius (1911) divided the sigmoid colon and re-anastomosed the proximal segment into the rectum in an end-to-side technique. The ureters were then implanted into the blind pouch of the sigmoid above the point of sigmoidorectal anastomosis. Heitz-Boyer and Hovelacque in France (1912) divided the sigmoid colon and brought the proximal segment out to the surface beneath the rectal sphincter alongside the anus. This procedure left the intact rectum and pelvic colon as a blind pouch also controlled by the anal sphincter and the ureters were transplanted into the pouch. Cuneo in Paris (1912) did a similar procedure but brought down an isolated segment of terminal ileum to form the blind pouch for the implantation of the ureters. In Russia, Diakonow (1908) proposed the formation of a tunnel of bladder mucosa from the trigone extending through the perirectal space to pass beneath the anal sphincter and drain the closed bladder to the skin of the perianal region. There is little wonder that in 1916, Battle Malone should write of exstrophy of the bladder, "The pathology is as vague and indefinite as the remedies are numerous and worthless."

Present day attitudes of therapy are a direct result of the publications by Coffey (1929-1933) who developed a more successful principle of diversion of the urinary stream. The various techniques of ureterosigmoid anastomosis as further improved by Jewett, Higgins and others have contributed much to reduction in operative mortality and immediate postoperative morbidity.

In spite of the zeal exhibited in the literature for reporting cases of exstrophy and methods of uretero-intestinal anastomosis, the long term morbidity and mortality remain very much in doubt. The most recent report is that of Hirsch and Thompson who were able to trace 128 patients with exstrophy following the Mayo-Coffey uretero-enteric anastomosis. There were 18 immediate deaths in 144 cases, or a hospital mortality rate of 12.5 per cent. Of 34 who died of known causes after leaving the hospital, 27 were of renal failure. A follow up appraisal of the condition of their survivors showed that 69.9 per cent gave a history of pyelonephritis. These authors were able to study 41 patients with subsequent excretory urograms (a third were made during the first postoperative year). Considering that ureterorenal dilatation, nonvisualization, and the presence of stones indicated upper urinary tract disease, it is noted that only 5 of the 41 patients or 12.2 per cent had excretory urograms which were normal and showed no evidence of obstructive phenomena. Walters from the same clinic in 1934 stated that of 85 transplantations only 13 had lived more than 10 years. A study of the literature for the past 60 years indicates that only 42 other patients have been reported to live more than 10 years after uretero-intestinal anastomosis. Exactly half of these lived more than 20 years after operation. A critical examination of these latter 21 surviving more than 20 years reveals that 1 patient lived 44 years before death in renal failure and only 6 others lived longer than 25 years. In all of the group in which autopsy was performed, death in every case was reported as due to renal insufficiency. Among the 21 survivors hydrom

by its inability to dilate beyond a certain point. Thus during conditions of extreme osmotic diuresis, the ureteral muscles are stretched to a stage where the contractile power is no longer manifest, and the ureter becomes a simple dilated tube through which urine continuously flows.¹⁰ It is at this stage that the resistance offered by peristalsis disappears, and the progressive elevation of pelvic pressure with increasing urine flow ceases.

SUMMARY

The response of the ureter of the dog to changing urine flow was investigated in trained unanesthetized animals by direct observation of peristaltic activity and graphic recording of peristaltic waves. Changes in pelvic pressure during variations in urine flow were also studied.

During increasing urine flow, the vigor of ureteral peristaltic contractions increases but the frequency of peristalsis remains constant, except during marked diuresis when the frequency decreases. The pressure within the renal pelvis also increases with urine flow, except during extreme osmotic diuresis, where it reaches a fixed upper limit despite further increases in flow. At this diuretic stage, the ureters behave as simple dilated tubes allowing urine to pour out in a continuous stream.

The authors are indebted to Dr. Chester Hampel and Dr. Domingo Gomez for their help in the preparation of this work.

should have a life expectancy equal to a comparable portion of the general population, while the average patient with cancer of the bladder can hope for less than 5 years of life. From a purely sociologic viewpoint, the child of 5 years who undergoes ureterosigmoidostomy and dies in uremia 30 or less years later cannot be said to have been transformed into a productive member of society by his operation.

With these facts in mind we have attempted to re-evaluate the present concepts of treatment of exstrophy of the bladder and to regard these children as an entirely separate category of disease from the adult with bladder cancer. Not only must the child have an immediate good result that will make him socially acceptable but he must look forward to a life free of recurrent urinary tract obstruction, infection and insufficiency.

The two primary factors in the progressive renal insufficiency that follows uretero-intestinal anastomosis seem to us to be ureteral obstruction and infection. It also seems obvious that ureteral obstruction will eventually result from mobilization of the ureter and implantation into the colon regardless of the technique employed, since some degree of cicatrization is inevitable. The human colon cannot be sterilized so long as it serves its function of a fecal reservoir and it makes little difference whether organisms reach the kidney by reflux up the ureter or by peri-ureteral lymphatic channels, pyelonephritis is the end result in either case. The problem resolves itself into devising a procedure that retains the advantages of the ureterosigmoidostomy and the utilization of the rectal sphincter but which does not require mobilization or disturbance of the ureters at any point. Diversion of the fecal stream from the rectal segment of bowel selected as a urinary reservoir is necessary to effect the most ideal situation and function of the urinary tract, that is, one that will result in a normal life expectancy.

OPERATIVE PROCEDURE

The concept of this operative procedure from which an entirely normal life expectancy should result is as follows. The exstrophy is left undisturbed until approximately 5 to 7 years of age. Beyond this age the psychological impact of the exstrophy begins to be apparent. The first procedure is a permanent type of colostomy performed at the junction of the lower and middle thirds of the sigmoid with complete closure of the distal stump. Two weeks later an attempt is made to sterilize the blind rectosigmoid by means of instillations and enemas containing antibiotics. The operative technique in the next step is as follows. An approximately 4 cm. longitudinal incision dividing the trigone is made through the base of the bladder. This is carried through the entire bladder wall exposing the anterior surface of the rectum and entering the cul-de-sac of the peritoneal cavity at this point. The posterior surface of the bladder at the upper end of the incision is then sutured to the anterior surface of the sigmoid with fine catgut so as to completely extraperitonealize the anterior wall of the sigmoid posterior to the bladder. A similar 4 cm. vertical incision is next made through the wall of the rectum immediately contiguous to the above incision in the trigone. These incisions are in the midline and approximately 2 cm. mesial to both ureters. There is no

of any kind calcuosis, tonic overdistended bladders are only few instances in which the meticulous urologist has sacrificed and still sacrifices many lamps in his futile efforts to get a better light

By using entirely imperfect and inadequate means the writer has made only few rough attempts to transilluminate the bladder cavity and the results were encouraging so that he felt authorized to publish this preliminary note and in the mean time equipped with more appropriate means to continue the experiment in the hope that he shall be able to report on it at a later date

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it then becomes a small diverticulum on the anterior rectal wall into which the completely undisturbed ureters and the normal ureterovesical junctions terminate (fig 3) With such a wide aperture or fistula constructed between the trigone

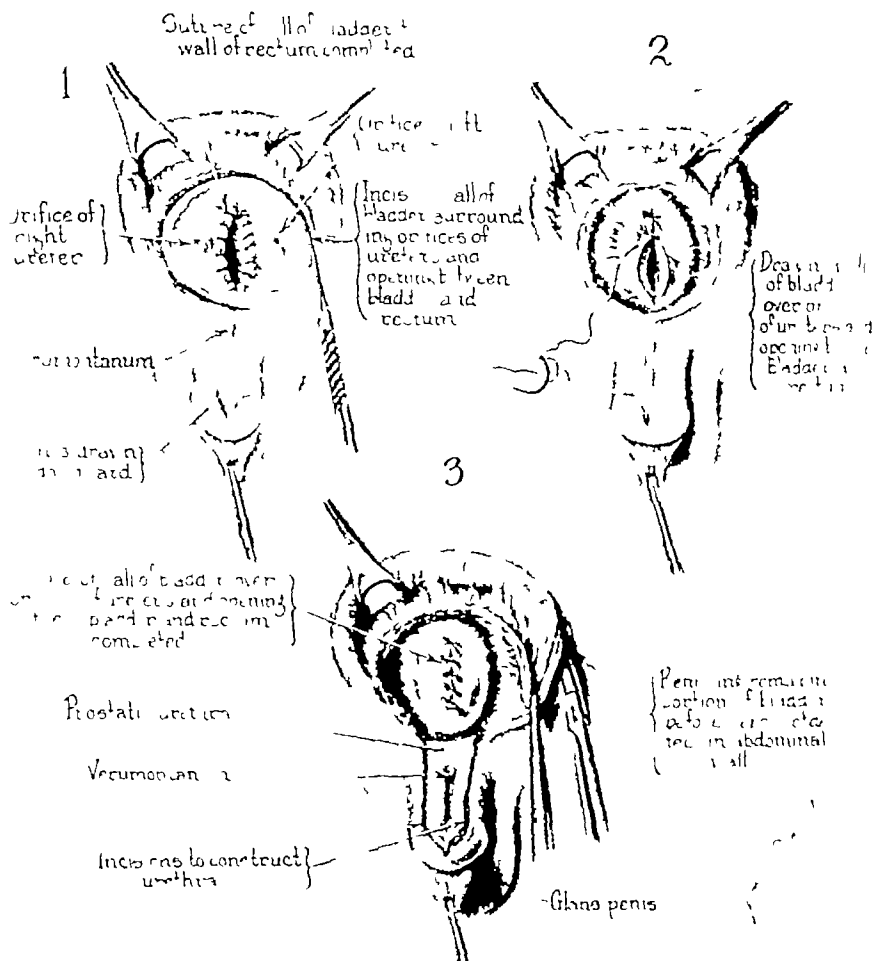


FIG 2 In 1, anastomosis resulting in a stoma between trigone and rectal cavity has been completed. Terminal ureters and ureteral orifices have been undisturbed. A circular incision is now being made around entire trigone and ureteral orifices. In 2 margins of the above circumscribed area are being turned inward and sutured thus closing bladder over newly established communication between bladder and rectum. 3 Closure of above area completed and beginning excision of remainder of extrophied or exposed bladder. Ureters now terminate in a small closed cavity which is a diverticulum on the anterior rectal wall. Mucosa of epispadiac penis is next closed in form of a urethra for purposes of ejaculation. Following this, corpora are brought together over constructed urethral lumen.

and rectum, there should be no stasis of urine in the miniature bladder or rectal diverticulum. The sphincteric control is of course by the rectal sphincter. The remainder of the mucosa of the bladder is then excised leaving the muscular bladder wall intact which is sutured as a buttress over the above closed miniature bladder or trigone or what is now a rectal diverticulum. This bladder muscle

Poer¹ stated there were approximately two thousand soldiers and five hundred Navy personnel who received spinal injuries in World War II. He further stated that the mortality during the Balkan wars was approximately 95 per cent, with an average mortality for the other wars since then of 50 to 60 per cent. Further, in World War II for the American Armed Forces, the mortality was approximately 20 per cent. Poer felt that this immediate improvement in mortality statistics was due to the availability of neurosurgeons in the forward field units. As can be seen, if the patients did not die during the early phases, they could easily be returned to continental United States for more definitive care.

On April 1, 1946, the Veterans Administration took over the group of paraplegics from the Army, and the Vaughan General Hospital became part of the Hines Veterans Administration Hospital. The average daily census on the Paraplegic Service since April 1, 1946 has been approximately two hundred and fifty-one patients. From April 1, 1946 to September 1, 1949, there have been 506 cases of paraplegia who have been worked up, hospitalized for awhile, and discharged from the Veterans Administration Hospital at Hines. Many of the patients tend to become relatively permanent guests because of inadequate housing facilities for a wheelchair existence. However, many, during this period, have finally obtained housing facilities and been discharged. Some have returned for further care, but the figure 506 represents different individuals and not different admissions. This review covers the 506 cases, regardless of the number of admissions anyone may have had.

The causes of the paraplegic state among the 506 cases fall into two prominent groups: the traumatic paraplegic and the nontraumatic paraplegic. To many of you the traumatic group is the one usually pictured in your mind when you speak of a World War paraplegic, but as you can see, there are many nontraumatic paraplegics. A breakdown of the 506 cases shows that 361 cases were due to trauma. 34 cases were due to myelitis which was a residual of an inflammation, such as encephalitis, meningitis, and the like. 7 cases were due to severe poliomyelitis with its residual. 6 cases were due to hemangioma of the central nervous system. 6 cases were due to multiple sclerosis, 24 cases were due to tumor of various types, and 68 cases were due to unknown causes. Of the 506 paraplegics, 36 were discharged because of death.

Riches studied 35 cases in England after World War II. Of these, 10 died within 2 years for a percentage of 28 per cent. The 10 deaths were due in 5 instances to toxemia which included urinary sepsis, one due to surgery, two due to accompanied pulmonary disease, one due to secondary carcinoma, and one due to multiple injuries. Guttman² stated that urinary infection is still the main cause of death among the paraplegics and represents a problem which, in spite of all efforts, is still unsolved. He felt that neither suprapubic cystostomy nor urethral catheterization has proved a safeguard. He reviewed 177 cases of traumatic paraplegia in which there were 13 deaths, 7.3 per cent, within 19 months after V. E. Day. Rappaport³ reported 6 deaths, five of which were due

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² Guttman I. *Proc Roy Soc Med* **40**: 219-232, 1947.

³ Rappaport H. *J. A. M. A.* **129**: 165-166, 1945.

closure of the skin in the lower abdomen and pubic area. Except for the scar this gives the patient the appearance of an entirely normal external genitalia and pubic area.

Since this procedure leaves completely undisturbed the ureteral orifices and intramural and terminal ureters and diverts the fecal stream, there should be a normal expectancy of life as far as the urinary tract is concerned. Any colostomy is undesirable and if it becomes a problem in later life, re-establishment of the fecal stream can easily be accomplished. This would add the hazard of feces to the urinary reservoir and might result in pyelonephritis and its late sequelae. It seems to us that continuation of the colostomy would be a lesser evil than the hazard of upper urinary tract complications when feces and urine are mixed in the same reservoir. The above procedure was accomplished so satisfactorily in a recent



FIG. 4. Genitalia before operation. Note moderately wide diastasis of recti muscles and nonunion of symphysis. Epispadic penis is pulled downward to fully expose exstrophy of bladder. Case 1.

case that the authors felt it worthwhile to report an early result employing this concept of treatment for exstrophy of the bladder.

CASE REPORTS

Case 1. An intelligent 9 year old boy, K. J. F., University of Virginia Hospital No. 299206, was admitted in July 1950 with typical exstrophy of the bladder (fig. 4). An excretory urogram showed normal kidneys and ureters (fig. 5). The previously described operative technique, both in forming a colostomy and construction of the rectosigmoid-trigonal reservoir leaving the ureters entirely undisturbed, was performed (figs. 1, 2 and 3). Convalescence was uneventful and there was no postoperative elevation of temperature and no pain or tenderness in the flank or other evidence of pyelonephritis. Blood urea determinations made one to two times weekly for four months after operation varied between 18 and 30 mg. per 100 cc. (Upper limits of normal by this method 45 mg. per 100 cc.) Blood chloride level and plasma carbon dioxide combining power remained within normal limits during the period of observation (table 1). During the operative period and early convalescence the patient was given streptomycin and penicillin.

having been made. In all 25 instances, the urine cultures showed urinary sepsis. None had a sterile urine. In the 11 cases in which no urine cultures were obtained, the patients were paraplegics as a result of the nontraumatic state. The most common organism to be cultured from the urine was *Aerobacter aerogenes*, while the second most common organism was *Pseudomonas aeruginosa*. The third most common organism cultured from the urine was *Proteus morgani*, while the fourth most common organism was *Bacillus coli* and the fifth *Streptococcus fecalis*. In most instances, the urine culture revealed at least three of these five organisms to be present. In many, all five organisms were present at the same time.

We have wondered about this distribution of the type of organism in the urine. Does it come from the bowel or does it come from the decubitus ulcers? These patients receive sulfa drugs and antibiotics freely. Does this fact change the predominant organism? An analysis of stool cultures in a small group of well-adjusted paraplegics shows *Escherichia coli* as the predominant organism with *Aerobacter aerogenes* second and *Streptococcus fecalis* third. An analysis of the cultures of decubitus ulcers from fifty different living paraplegics shows the predominant organism was hemolytic *Staphylococcus aureus* while *Proteus vulgaris* was second and one of the *Pseudomonas* group was third. An analysis of urine cultures from 20 cases of paraplegia with automatic bladders shows none were sterile. The predominant organism in this group was *Aerobacter aerogenes*, and one of the *Pseudomonas* group was almost equal to it. This agrees with the cultures of urine in the group who died but does not agree with the cultures of bowel or decubitus ulcers.

It is our belief that these patients have an infecting organism in the urine that is very resistant to all sulfa drugs and all antibiotics. These patients are given these medications freely every time they have a septic temperature. The result is, that even though the temperature may not be due to the urinary tract, there is incrimination of susceptible organisms in the urinary tract and a survival of the resistant ones. Thus when a severe urinary tract infection flares up, it is due to a very resistant organism.

CASE REPORTS

Let us now review the 11 cases of traumatic paraplegia in which death was due to uremia.

Case 1. J. B. At the time of his injury in February 1945, it was necessary to remove the left kidney. In June 1945, he had a staghorn calculus in his remaining kidney. This was not removed. Renal function tests in February 1946, showed very little excretion of either phenolsulfonphthalein or diodrast. Furthermore, the patient had had bladder catheter on two occasions—once in July 1945, and again in December 1945. During his paraplegic state he had had an indwelling urethral catheter with closed drainage all the time. In March 1946 the nonprotein nitrogen was 77 and in April 1946 it was 111. He died April 16, 1946 fourteen months after his injury. No autopsy was obtained. As can be seen, the patient had a staghorn calculus in a poorly functioning solitary kidney.

Case 2. A. B. had had several episodes of pitting dependent edema which had

by means of the rectal sphincter. The capacity of the rectosigmoid (fig 6, A) is approximately 300 cc so that he can go many hours without emptying. Postoperative excretory urograms 10 months later revealed an entirely normal upper urinary tract (fig 6, B) as was present before operation. The concentrations of blood urea, plasma chloride, and plasma carbon dioxide combining power remained within normal limits over 4 months' observation (table 2). The patient in effect has a normal and sterile upper urinary tract. He seems to be perfectly happy with the colostomy (fig 7) and is attending school for the first time. The colostomy functions only once daily and he does not wear a rubber receptacle.

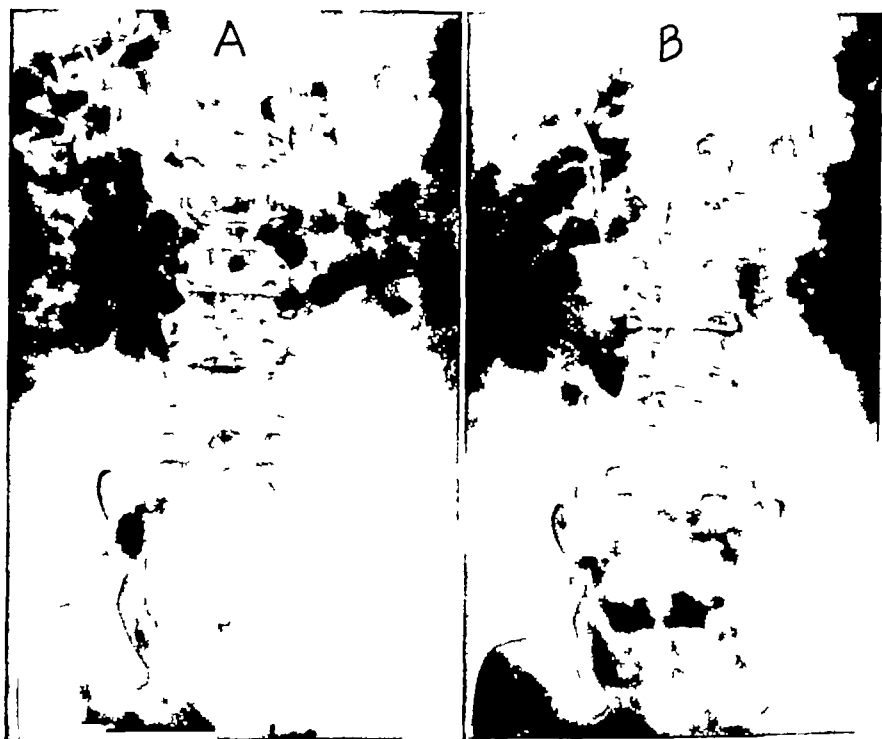


FIG. 6-1, illustrating lower isolated rectosigmoid portion of bowel after injection of contrast medium. No evidence of reflux up ureters and receptacle is capacious for interval voidings of 3 to 4 hours. B, excretory urogram 10 months postoperative. Kidneys and ureters are entirely normal without evidence of any change. Colostomy shadow is visible in left midabdominal region. Case 1.

Life expectancy with the normal urinary tract and especially with sterile urine should be normal.

Case 2 B. R. W., U. Va. Hosp. No. 312996, an intelligent, well developed 10 year old girl with incontinence of urine and feces due to complete exstrophy of the bladder and prolapse of the rectum was first seen on June 19, 1951. She had been examined at other institutions and told that her situation was hopeless because of the prolapsed rectal mucosa. The child exhibited the shyness and reticence common to patients with exstrophy. There was wide separation of the pubes and diastasis of the recti muscles with complete exstrophy of the bladder.

June 1947, a right perirenal abscess was opened. Marked ascites and edema developed. The nonprotein nitrogen rose to 93. The albumin-globulin ratio was reversed. He died 27 months after injury. At autopsy examination, one kidney weighed 650 gm., while the other weighed 450 gm. The cut section revealed a normal architecture to be replaced by smooth, homogeneous, yellow, firm tissue of amyloid. Microscopically, there were very few glomeruli left.

Case 7 C R J was injured in November 1942, and lived for 68 months. A right renal calculus was not removed. He had many attacks of pyelonephritis. He had a suprapubic cystotomy for a long period of time, but this was allowed to close. Following this, the bladder was drained by means of an indwelling urethral catheter. In May 1947, he started to vomit and become oliguric. The nonprotein nitrogen slowly rose to 131. He died in uremic coma. No autopsy was obtainable.

Case 8 W T J was injured in April 1945. In October 1945, stones were removed from the left kidney. A laminectomy was done in November 1945, and a cordotomy was done in December 1945. The cordotomy was repeated in February 1946, and again in August 1946. The nonprotein nitrogen in June 1946, was 74. By November 1946, it was 130. The patient died after 19 months of paraplegic state. At the autopsy examination, there were dense adhesions around both kidneys. There was an abscess around the right kidney which involved the second and third lumbar vertebrae. Both renal pelves were full of a thick mucoid urine. The renal capsules could not be stripped without tearing. On cut section, it was difficult to tell the renal cortex from the medulla. The thickness of the cortex and medulla together was only 1.3 cm. On microscopic examination, there was a great deal of infiltration around the tubules by white blood cells, both polymorphonuclears and lymphocytes. It was believed that this was an example of bilateral pyelonephritic contracted kidneys.

Case 9 H B P was injured in August 1944, and lived 25 months. He was in several hospitals. When received at Hines in May 1946, he was found to have a right renal calculus, but he was too sick to be considered for surgery. The nonprotein nitrogen was 111. The right kidney was catheterized, and frank pus was obtained from the right renal pelvis. The patient continued to become worse and died in September 1946. No autopsy was obtainable.

Case 10 H P was injured in April 1945. He had an immediate laminectomy. A suprapubic cystotomy was also done. In June 1945, a left pyelolithotomy was done. A *Bacillus proteus* infection developed in the incision. In October 1945, a right pyelolithotomy was done, and a large perirenal abscess found. The patient later had a severe hemorrhage from the right kidney requiring a right nephrectomy 3 days later. In November 1945, a second pyelolithotomy was done on the left and a permanent nephrostomy was done. In spite of this another calculus developed in the left kidney. In December 1946, an abscess was drained from the old right nephrectomy site. Following this, the nonprotein nitrogen began to slowly climb. In January 1947, it was 73, and in June 1947, it was 92. He died June 27, 1947. At the autopsy examination, the left kidney contained a large staghorn calculus, and the left renal parenchyma had many small abscesses. There was very little renal tissue left.

Case 11 R S was wounded in September 1944. He got along fairly well ex-

proposed vesicorectal anastomosis. It was our considered opinion that a normal life expectancy was more important than reproduction. The postoperative course

TABLE 3 *Blood electrolyte patterns and cultures Case 2*

DATE	BLOOD UREA	PLASMA CHLORIDE mEq/l	PLASMA CO ₂ mEq/l	DIET	CULTURE FROM RECTAL POUCH	SYMPTOMS OF ACID
6/20/51	46	98.3	21.2	Low residue		
6/27/51	Operation—Formation of rectal pouch					
7/5/51	18	99.4	22.6	Regular	Sterile Cult	No
7/6/51	Operation—Vesicorectal anastomosis					
7/10/51	20	101.7	22.5	Regular	Smear Negative	No
7/14/51	25	103.5	23.9	Regular	—	No
7/17/51	32	98.3	20.3	Alkaline Ash	Smear Negative	No
7/20/51	20	101.7	23.6	Alkaline Ash	—	No
7/23/51	25	101.1	21.2	Alkaline Ash	Smear Negative	No
7/25/51	38	106.9	20.7	ACID ASH	Sterile Cult	No
7/27/51	20	106.9	20.5	ACID ASH	Sterile Cult	Mild Nausea
8/16/51	16	103.5	15.6	Regular	B. proteus	Yes—Marked
11/16/51	24	98.3	25.8	Alkaline Ash	Sterile Cult	No
3/13/52					Sterile Cult	



FIG. 8 Excretory urogram 5 months after operation demonstrates normal calyces and pelvis without obstruction. Case 2.

was uncomplicated and after daily irrigations and insufflations of the lower rectum with aureomycin cultures from this pouch became sterile. On July 6, a

because of osteomyelitis. In December 1946 he had a presacral neurectomy and in February 1947 he had a bilateral cordotomy. His neurologic lesion is at a level of D-11 and is physiologically complete. The patient had daily episodes of a very low-grade fever. Investigation revealed that he had severe bladder spasms that on occasion would force the catheter out. Furthermore the cystogram revealed bilateral ureteral reflux. He suffered a recurrence of the ischial osteomyelitis. It was believed that the osteomyelitis caused an inflammation around the bladder neck which was accentuated by means of the indwelling urethral catheter. In June 1949 a suprapubic cystotomy was done and is still functioning well. It is planned to leave the patient for an indefinite period with a suprapubic cystotomy. Since that form of urinary drainage was established the patient has not had any episodes of fever. He still has decubiti but the patient himself

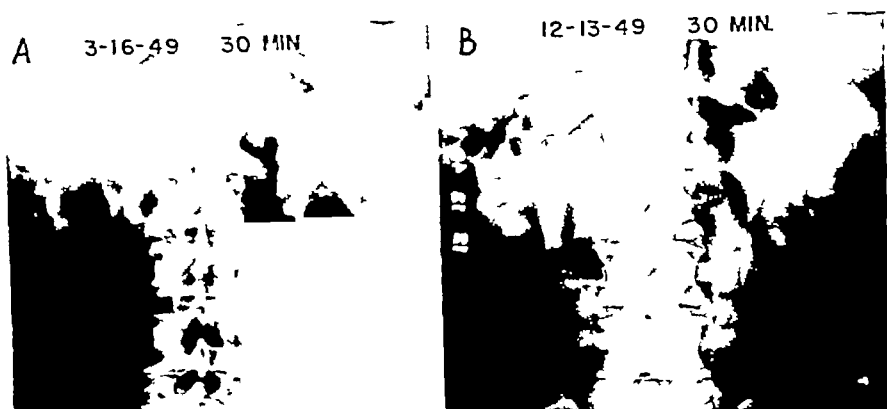


FIG 1

feels much improved and is personally well pleased with the suprapubic cystotomy. With a suprapubic cystotomy he has been able to attend classes in a neighboring college.

(*Case 3*) E. W. This 51 year old patient was wounded October 4, 1947. He had an immediate laminectomy. Examination revealed a paraplegic with complete lesion from L-2 down on the right and from L-5 down on the left. Thus he had essentially a cauda equina lesion. At first his bladder was drained by an indwelling catheter. After a few weeks this was removed and he was put on external type of urethral drainage. He seemed to empty his bladder but it required a great deal of straining. He had several episodes of decubitus ulcer formation over the sacrum and trochanters. In early 1949 the routine blood chemistry revealed nonprotein nitrogen of 115 with a urea nitrogen of 70. For some reason this had not been checked for several months. He had seemingly been getting along well. The residual urine was checked and it was found to be 125 cc of thick foul smelling urine. Closed urinary drainage with an indwelling catheter was restored and the nonprotein nitrogen slowly subsided to 55 where it became stabilized. Cystoscopic examination revealed definite evidence of early trilobar prostatic hypertrophy. A transurethral resection of the prostate and bladder neck was done in October 1949. The patient got along well. The catheter was

it is an extremely remote possibility that there would be any increased incidence of malignancy in the small remaining portion of the bladder wall of cases subjected to the above reconstructive technique.

SUMMARY

The most ideal repair of exstrophy of the bladder should be a surgical procedure in which the patient could look forward to a normal life expectancy.

No evidence is available that transplantation of the ureters at any age in exstrophy of the bladder would lead to a normal expectancy of life. On the contrary, early and late results following ureterosigmoidostomy are uncertain.

An operative technique is presented to divert the urine into the rectosigmoid for exstrophy in which the cardinal feature is nondisturbance of the lower and transvesical ureters and ureteral orifices. In this way late cicatricial and obstructive changes in the terminal ureters are avoided and the incidence of ascending infection should be greatly minimized. Indeed permanent sterilization of the urinary tract may be possible. The hazard of ascending pyelonephritis would be greatly reduced by the maintenance of the permanent colostomy which is a lesser evil than the complications which may result in the upper urinary tract when the urine is diverted in conjunction with the fecal stream. The colostomies in the two children have not given the least difficulty. Each functions only once a day and the boy even refuses to wear a colostomy cup stating that it is unnecessary.

CONCLUSION

It is our belief that any operative procedure involving mobilization of the ureters is subject to a high incidence of upper urinary tract complications. A concept of management of exstrophy of the bladder involving nondisturbance of the ureters and ureterovesical valves has been presented. If the results in our cases can be reduplicated, then ureterosigmoidostomy and various trigonal transplantations for exstrophy, especially in the first few months of life, are not indicated.

The operation is adaptable to some cases of incontinence following sphincteric injuries from various prostatic operations.

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A NEW CONCEPT CONCERNING TREATMENT OF EXSTROPHY OF THE BLADDER

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There are few chapters in the annals of surgery more intriguing than those dealing with exstrophy of the bladder. The challenge that these unfortunate children offer the surgeon has resulted in a large number of ingenious operative procedures and a voluminous literature on the subject. More than 400 articles dealing exclusively with exstrophy of the bladder have been published in the 100 years since Mr. Lloyd and Sir John Simon first attempted to divert the urinary stream into the rectum. The unfortunate results of both Lloyd and Simon may have deterred further attempts at the establishment of urinary-colic fistulas so that the emphasis on treatment during the next 40 years was primarily toward closure of the anterior wall of the exstrophied bladder. Trendelenburg attempted this by fracturing the sacro-iliac junctions and approximating the pubes in an effort to bring the bladder within the bony pelvis. Wood in America and Roux in France were contemporary names associated with methods of swinging skin flaps to close the bladder defect. The late Hugh Young developed a technique for closure of the bladder and reconstruction of the abdominal wall, penis and external sphincter. This most ideal rehabilitation procedure is prone to be followed by fistulas at the base of the constructed penis as a result of intra-abdominal pressure on the suture lines. It is only applicable in a small percentage of cases in which the abdominal wall defect is not large and in which there is not a wide diaphysis of the symphysis and recti muscles.

A revived interest in diverting the urinary stream above a competent anal sphincter followed Maydl's report (1894) of a method by which the trigone was mobilized, reversed and sutured into the anterior rectal wall. The widespread use of the Maydl procedure was reflected in a review of the literature by Morehead (1916) in which 152 cases were reported. At the same time Bergenhem in Stockholm (1894) and Peters in Canada (1901) were performing a somewhat similar operation in which the trigone was divided and the ureters with a surrounding cuff of trigonum transplanted into the rectum. These latter authors and their procedures have directly resulted in the development of our own present attitude toward therapy of exstrophy of the bladder. In the first two decades of the present century, however, many types of bizarre operations were reported with little more to recommend them than the author's ingenuity. Fowler (1898) and Movnihan (1906) were exponents of ureterorectal anastomosis in America. Verhoogen and Mikki (1910) isolated the cecum which was drained through an appendicostomy.

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LEIOMYOSARCOMA OF BLADDER REPORT OF CASE

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Primary sarcoma of the bladder is uncommon, a total of 158 cases having been noted in the literature to date. All histologic types have been described, one of the rarer being leiomyosarcoma, of which only 23 have been reported. Adequate summaries of the recorded cases of vesical leiomyosarcoma were made by Kretschmer and Doerhing in 1939,¹ Crane and Tremblay in 1943,² and Lev and Bell in 1947.³ The author wishes to report an additional case of leiomyosarcoma of the bladder.

CASE REPORT

H A, a white man, at the age of 56, first consulted the writer in 1937, complaining of urinary frequency, painful urination, and attacks of acute retention for the preceding 4 years. The previous history was negative. Urological study disclosed a slight degree of benign prostatic hypertrophy, contracture of the vesical neck, and an intense chronic cystitis. Residual urine measured 700 cc. On excretory urography both kidneys functioned well and the pyelo ureterogram was normal bilaterally. Neurological examination was negative. The blood Wassermann was negative and the spinal fluid was normal. The blood count and blood chemistry figures were also normal. Suprapubic cystostomy and, 2 weeks later, transurethral resection of the vesical neck, were performed at the Jewish Hospital, pathological report was benign hypertrophy of the prostate. The postoperative course was uneventful, the suprapubic fistula healed satisfactorily following removal of the suprapubic tube, and subsequently the patient voided well, there was no residual urine. In about 2 months the urine became clear.

He remained symptom-free for 11 years after operation, frequency of urination, dysuria, and pyuria then recurred. At that time he consulted another urologist, who diagnosed vesical calculi and performed suprapubic cystolithotomy in 1948. Subsequently there was considerable difficulty in urination, accompanied by a high residual urine, apparently the result of recurrent contracture of the vesical neck. Accordingly, transurethral resection was done by the same urologist, the pathological report was benign prostatic hyperplasia. The patient then voided more comfortably, but frequency and dysuria continued, and recently gross hematuria was noted. He then returned to my care, after a lapse of 13 years.

The patient was admitted to the Jewish Hospital on January 26, 1950. His general condition was good. Examination of the heart and lungs was negative. Blood pressure was 120/74. There were two well-healed suprapubic scars. No abdominal masses or viscera were palpable. On rectal examination the prostate was small, and its consistency fibrous. Residual urine varied from 360 to 960 cc. The urine was foul smelling, alkaline, and contained large amounts of pus, cul-

¹ Kretschmer H I and Doerhing P. Arch Surg 38:274 1939.

² Crane A R and Tremblay R G. Ann Surg 118:887 1943.

³ Lev M and Bell W J. J Urol 57:251 1947.

phrosis was reported in 16 and the information in the remaining 5 was indefinite. Elevation of blood urea occurred in 12 urinary tract calculus in 5 and perinephric abscess in 2. These are case reports from many different operative techniques but they are the best results on record, and are in accord with reports on life expectancy from those clinics where relatively large numbers of patients have been followed more than 20 years.

As far as longevity is concerned the foregoing results may indeed be no more superior than had the patients not been subjected to transplantation of the ureters. C. H. Mayo in 1925 made the statement that "statistically 50 per cent of all patients afflicted with congenital exstrophy of the bladder are dead by the tenth year and 66.6 per cent of them are dead by their twentieth year." He gave no data to support this impression. By comparative study of the literature there are 30 patients with exstrophy of the bladder who lived to the fourth decade or longer without benefit of surgery, 13 were in the fourth decade, 9 in the fifth decade, 6 in the sixth decade and 2 in the seventh decade. Each of these 30 individuals had lived longer than the longest reported survival following uretero-intestinal anastomosis (Stevens).

These figures are not contradictory to the many reports of satisfactory urinary tract function in 5 to 10 year results (Higgins), etc. There is, however, no guarantee that the patient with a satisfactory result in 5 to 10 years will continue to have adequate renal function for 20 or more years. The amount of trauma from obstruction and infection that the kidneys can absorb before clinical uremia intervenes is little less than amazing. The fact remains that of the many hundreds of children with exstrophy of the bladder in which some form of uretero-intestinal anastomosis was done since 1898, there is not one report in the medical literature of one of these attaining a normal life expectancy. Furthermore, every case report in which autopsy was done following death after 10 or more years of closed existence has shown the cause of death to have been renal failure without exception.

There is little in the scientific advances of the past half century to suggest that these results will improve in the foreseeable future because these are problems of long term recurrent insults to renal function. Modern surgical technique, chemotherapy, antibiotics and correct fluid and electrolyte balance can reduce the operative mortality and shorten the convalescence. These factors when promptly available may shorten the course and reduce the destructive effects of recurrent pyelitis but so long as the divided ureter is placed in the intact and unsterile colon there is every indication that late cicatricial changes occur at the site of implantation resulting in inevitable renal insufficiency.

There is little doubt that intracolic diversion of the urinary stream is the only method of social rehabilitation yet devised for the patient who must forego the use of a normal bladder and given the choice most individuals would prefer a somewhat shorter life of social acceptability to a longer one of constant uriferous odor and social ostracism. The problem of the child with exstrophy, however, is quite different from that of the adult with carcinoma of the bladder. The child

pubic scars and extended through the rectus fascia. Upon retracting the rectus muscles there was exposed a firm, smooth, extraperitoneal mass the size of a large grape-fruit. It was situated anterior to the bladder, which it displaced far posteriorly and to which it was densely adherent. On probing the sinuses in the skin they were seen to communicate with the mass. The latter was opened into and found to be made up of numerous irregularly-shaped fragments of tissue which were soft, pink and red in color, and varied in size from 0.5 cm. to 5 cm. in diameter, some of this tissue was necrotic in appearance. A small amount of pus, but no urine, was also present in the mass. Culture of the pus yielded non-hemolytic streptococcus and *B. proteus*. Following removal of the tumor fragments the suprapubic mass noted preoperatively was no longer visible or palpable. An attempt was made to thoroughly visualize the bladder, but this was not possible because it was so firmly encased by cartilage-like adhesions. With considerable difficulty only a small portion of the anterior bladder wall could be exposed, the bladder was opened into, but because of its poor accessibility the interior could not be explored satisfactorily. A cystostomy tube was inserted into the bladder and the site of the tumor was also drained.

The pathological report was as follows: "Histologic study reveals a tumor which is composed of short, plump, spindle-shaped cells with rather large, separately-placed nuclei with vesicular appearance, in some nuclei the chromatin is granular and prominent. Cell borders are indistinct and in places the cells appear to run into one another. In some areas the tumor cells stream out in short bundles, forming irregular, fan-like paddings. There are zones of necrosis present, and in these areas there are marked infiltrations with inflammatory cells. Thrombosed capillaries are also seen, as well as numerous newly-formed blood-vessels. Mitotic figures are frequently observed, and in some places atypism is noted. The Laidlaw connective tissue stain shows a delicate reticulum of fibers between individual cells and between groups of cells. In a phosphotungstic acid preparation occasional delicate fibrillae are seen within the cytoplasm of some of the tumor cells. Diagnosis: Leiomyosarcoma of bladder" (fig. 1).

Following operation the patient showed slight improvement for several days, then pursued a downhill course, becoming cachectic, progressively weaker, and suffering considerable suprapubic pain. Ten days postoperatively there was already evidence of tumor recurrence in the wound: a firm mass developed in the suprapubic area at the previous site of the tumor and a small, firm nodule appeared adjacent to the wound. Several days later additional similar nodules were noted in the area of the wound: the nodules later ulcerated through the skin. The patient's condition now deteriorated rapidly and he expired on the seventeenth postoperative day.

At autopsy the pertinent findings were confined to the urinary tract (fig. 2). The bladder was thickened and trabeculated, and its mucosa intensely inflamed. Arising from the dome of the bladder and extending down the anterior and posterior walls, was a large, necrotic tumor which occupied about two thirds of the bladder lumen, its base measured 8.0 cm. in diameter. The tumor was pink, soft and friable. At the roof of the bladder the neoplasm extended diffusely through

exposure or disturbance whatever to the ureteral orifices or any portion of the ureters

An anastomosis is next made between the bladder and the aperture or opening in the rectosigmoid somewhat in the manner of a gastrojejunostomy, bringing mucosa to mucosa (fig 1) A fistula is thus established between the midtrigonal

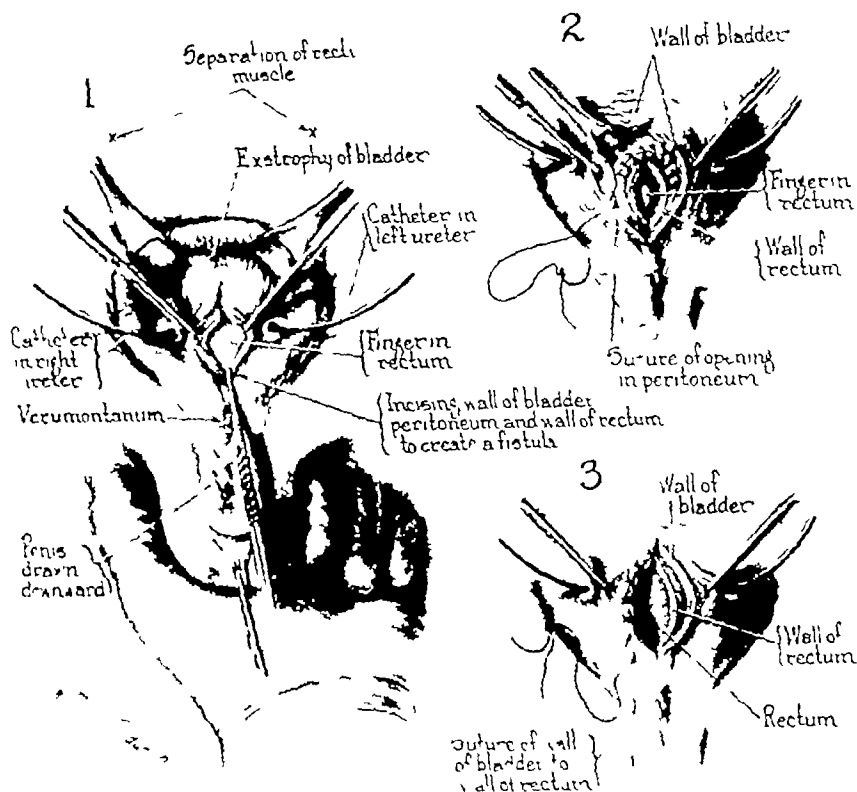


FIG. 1. Vertical incision in trigone of bladder as first step to rectovesical anastomosis. Note that incision is midway between ureteral orifices which are undisturbed. After division of entire bladder wall a similar incision is made into interior wall of rectum. These incisions at this point open cul de sac and expose peritoneal cavity. In 2, a continuous catgut suture is used to close peritoneal opening at this point. In 3, a continuous suture of catgut is used to complete a mucosa to mucosa anastomosis between floor of bladder and rectum.

region of the bladder and the interior surface of the rectum. A circular incision is then made around the entire base of the bladder (fig 2) well away from the ureteral orifices. This incision isolating the trigone (and trigonal-rectal fistula) is carried through the entire bladder wall with the exception of the peritoneum. This isolated bladder base is then closed with a continuous suture of chromic catgut. The capacity of this closed portion of the bladder is small and in actuality

the entire thickness of the bladder wall over a wide area, invaded the prevesical tissues and in several places extended to the skin, where it formed ulcerating nodules. Microscopic examination of the tumor revealed leiomyosarcoma, identical in appearance to the tumor removed at operation. A small amount of non-obstructing prostatic tissue was present at the vesical neck. Both ureter orifices were normal. There was a mild bilateral hydronephrosis, but the parenchyma of each kidney was essentially normal. Both ureters were normal in their entire course and there was no evidence of tumor encroachment on either ureter. There were no metastases either to lymph nodes or any of the viscera.

DISCUSSION

It is noteworthy that the diagnosis of sarcoma of the bladder is often missed preoperatively, frequently it is not made until autopsy. In the reported case the accompanying alkaline incrustated cystitis probably masked the underlying tumor, so that it could not be visualized cystoscopically. Cystography also commonly fails to disclose evidence of a vesical sarcoma, even when very large. In the case of leiomyosarcoma reported by Kretschmer and Doerhing,¹ for example, although the tumor filled the bladder cavity, the cystogram was normal.

An abdominal tumor is an unusual manifestation of sarcoma of the bladder. In the author's case the mass gave the clinical impression of prevesical abscess because of the long-standing severe cystitis and the recent development of fever, intense suprapubic pain, and lower abdominal sinuses which drained pus.

The fatal outcome in the case reported is the almost invariable result in bladder sarcoma regardless of the type of therapy employed. The tumor is extremely malignant and usually causes death within a year of the onset of symptoms.

SUMMARY

A case of leiomyosarcoma of the bladder, the twenty-fourth on record, is reported.

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supports the peritoneum and leaves relatively undisturbed the midline hernia formerly composed of the entire bladder

In performing the above procedure the distal portion of the trigone was divided transversely in order to close the bladder. The mucosa of the prostatic urethra then terminates in the proximal portion of the prostatic urethra. A urethra is next constructed using the mucosa on the floor of the epispadic penis. This urethra originates at the above divided trigonal mucosa in the proximal prostatic urethra and terminates at the normal position on the glans penis. The corpora

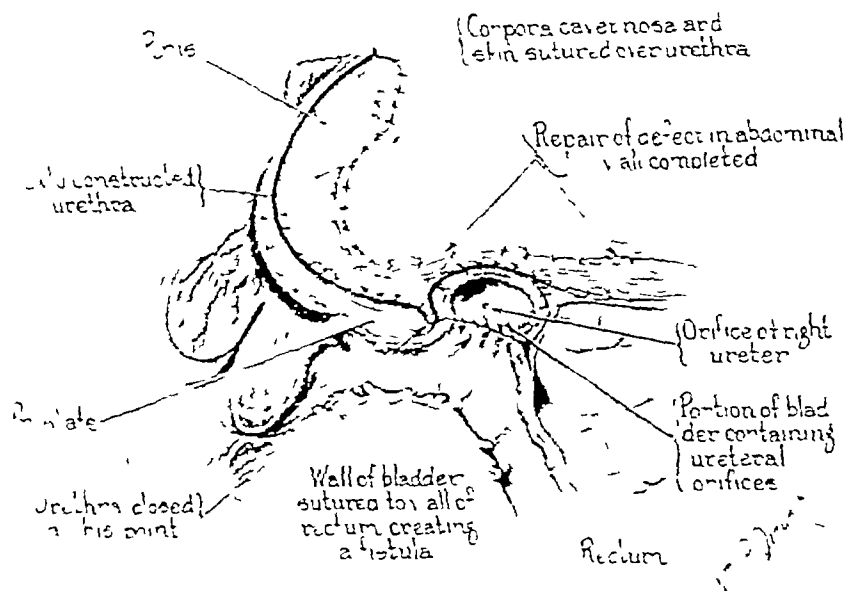


FIG. 3. Sagittal section shows newly constructed urethra which begins at proximal portion of prostatic urethra. Closed bladder cavity and undisturbed terminal ureters are also illustrated. Repair of abdominal defect has been completed by use of fascia of external oblique. With adequate communication between bladder and rectum urine flows unimpeded into rectal reservoir where continence is attained by use of rectal sphincter.

and skin are finally brought over this newly constructed urethra. The patient should be able to ejaculate from this constructed urethra which ends blindly at the divided vesical neck and proximal to the verumontanum.

The abdominal defect can be repaired by one of several methods. The recti muscles can be brought together in some instances in which the diastasis is not too wide. We have used flaps of fascia of the external oblique on occasion to act as a buttress over the defect. When there is no marked abdominal defect and herniation of the bladder, it has been possible simply to undercut the full thickness of the abdominal skin and bring this together in the midline thus effecting

Sections from the cystic mass showed a thin fibrous wall with no recognizable lining epithelium. At the junction with the solid mass there were many bizarre shaped glands lined by tall columnar epithelium with considerable mucus pre-



FIG. 1 Gross specimen. A, intravesical portion of carcinoma, B, extravesical portion, C, cyst wall opened, and D, gelatinous contents of cyst.



FIG. 2 Section of bladder showing A, transitional epithelium of mucosa, B, invading adenocarcinoma.

ent. The glandular epithelium was moderately pleomorphic with many of the cells showing hyperchromatic nuclei. Invasion of the muscular layer of the urinary bladder was present and the neoplasm extended up to immediately beneath the transitional epithelium of the bladder. Small groups of anaplastic cells were seen in endothelial lined channels in one area. Vascularity was moderate.

cillin and after removal of the rectal tube a course of terramycin. At the beginning of the third month and after discontinuation of all antibiotics we were able to



FIG. 5 Excretory urogram before operation shows kidneys and ureters to be normal without any indication of pyelonephritis. Case 1

TABLE I *Cultures from isolated rectum Case 1*

DATE	CULTURE
S 5-50	Operation—Formation of rectal pouch
S 9-50	B. coli
	B. aerogenes
S 12-50	Staph. aureus hemolyticus
	Staph. albus nonhemolyticus
S 14-50	Sterile
S 15-50	Operation—Vesicorectal anastomosis, closure of bladder
S 18-50	B. coli
	B. aerogenes
S 21-50	B. coli
	B. aerogenes
10 2-50	Sterile
Antibiotics discontinued	
10 16-50	Sterile
10 23-50	Sterile
11 13-50	Sterile

obtain cultures of the urine from the rectum on four occasions at weekly intervals and these were all sterile. The patient was discharged from the hospital in excellent condition with a perfectly functioning colostomy having only one movement a day which the child himself handled entirely. Urinary continence was normal

A NEW FEMALE AIR CYSTO-URETHROSCOPE

DAVID W. GODDARD

Many urologists find it necessary from time to time to treat the female urethra, bladder neck, and trigone with medications directly through an air cysto-urethroscope.

It readily is recognized that those men who confine their work to female urology, frequently in conjunction with gynecology, and do practically all of their work through air cysto-urethroscopes find themselves completely at home with these instruments, and apparently find them adequate in all respects, however, those urologists who do all of their diagnostic cystoscopies and ureteral instrumentations with the modern water cystoscopes, as we do, probably have found, as we have, that the currently available female air cysto-urethroscopes leave a certain amount to be desired in the matter of good visualization.

That Dr. Howard A. Kelly, the late chief of the Departments of Gynecology and Female Urology at the Johns Hopkins Hospital, went through an evolutionary process in the development of the modern Kelly air cysto-urethroscope is attested to by his early writings. In 1893, he first described his direct view endoscope. In 1894, he stated that the ideal instrument was 8 cm. long, equal in diameter from end to end, and had a diameter of 1 cm. In his classical textbook, written with Burnam and published in 1914, Dr. Kelly stated "The best instrument for inspection of the urethra is a short speculum of an average size, about one centimeter in diameter and four and one half centimeters in length." Surely the fact that expertness with an instrument comes from its constant use accounts for the fact that Dr. R. W. TeLinde, present chief of the Departments of Gynecology and Female Urology at the Johns Hopkins Hospital writes me "I am amazed at the quotation which you dug up from Dr. Kelly stating that the ideal instrument was $4\frac{1}{2}$ cm. in length. The regular female Kelly cystoscope which we have used for years is a little over 12 cm. in length. We also have a few extra long cystoscopes which are $17\frac{1}{2}$ cm. in length, but for all practical purposes the one of slightly more than 12 centimeters seems to be about the right length and certainly the one which we use daily."

For a number of years at Duke Hospital the Kelly cysto-urethroscope was used and, although it was found usable enough, almost every one of the new house officers coming along had some difficulty with it because of its "gun barrel" vision. We all were delighted when our armamentarium was augmented by the addition of two Koch cysto-urethroscopes, sizes 30F and 32F, because the shorter length improved our vision. The addition of a handle, see photograph, made the Koch even more satisfactory, and the proof of its superiority over the Kelly in our hands lay in the fact that, in a short time, every one of us was using the Koch in preference to the Kelly.

After using the Koch for some time certain inadequacies became apparent.

Read at annual meeting, Southeastern Section, American Urological Association, Memphis, Tenn., March 9, 1951.

The rectal wall and mucosa were observed to protrude 5 inches outside the anal sphincter. We noted that she had a definite rectal sphincter after reduction of the prolapse although the tone and ability to contract was diminished due to the long duration of the condition. Excretory urograms revealed normal pelvis,

TABLE 2 *Blood urea and electrolyte concentration before operation and after formation of trigono rectal pouch Case 1*

DATE	BLOOD UREA	PLASMA CHLORIDE mEq./l.	PLASMA CO ₂ mEq./l.
7-31-50	39	98.4	22.6
8-5-50	Operation—Formation of rectal pouch		
8-14-50	27		23.9
8-15-50	Operation—Vesicorectal anastomosis, closure of bladder		
8-18-50	29	93.2	
8-21-50	24	103.5	24.8
8-28-50	32	96.5	23.2
9-4-50	29	101.2	22.6
9-18-50	26	99.7	24.4
10-2-50	18	105.2	22.4
10-30-50	24	102.6	19.3
11-13-50	30	107.7	20.4
Normal Values	25-35	97-106	23-27



FIG. 7. Illustrating postoperative result. Colostomy which functions only once daily in excellent condition. Well healed suprapubic scar is without evidence of herniation. Once epispadiac penis is almost normal in appearance and contains a normal caliber urethra which ends blindly in proximal portion of prostatic urethra. A small rubber catheter can be easily passed to prostatic urethra. Ejaculation should be normal. Case 1.

kidneys and ureters. The blood urea, urea clearance, plasma carbon dioxide, and chloride concentrations were all within normal limits.

On June 27, after proper preparation the sigmoid colon was divided at the junction of the middle and lower third and a permanent colostomy formed with the proximal segment. The distal segment was closed to form a blind rectosigmoid pouch. After deliberate consideration it was decided to remove the uterus in this case because the later growth of this organ might become a hazard to the

1) Lack of a handle made it difficult to manipulate, this was overcome by having a handle put on in our brace shop, see photograph 2) The flat presenting surface requires that the operator take his eye off the site to be treated in order to insert working instruments into the lumen of the "scope." Both of these inadequacies were corrected in the Kelly, which has a very usable handle and which has a funnel-shaped presenting part that permits the operator to introduce the working instruments without taking his eye off the part to be treated.

It seemed obvious, therefore, that an instrument which combined the best features of both of these instruments and eliminated the bad features of each would have the greatest usability in the hands of those of us who are primarily "water cystoscopists."

Through the kind co-operation of Mr. G. M. Wallerich of V. Mueller and Company, Chicago this instrument has been made. In the accompanying photographs, from top to bottom, relative sizes of the Young male air urethroscope, Kelly female air cysto-urethroscope, Goddard female air cysto-urethroscope, and Koch female air cysto-urethroscope are shown. The instrument presented here has an over-all length of $9\frac{1}{2}$ cm. and a barrel length of only $7\frac{1}{2}$ cm. The light carrier is similar to that of the Kelly instrument and provides excellent illumination. We have it in sizes 30F and 32F, but larger or smaller sizes may be obtained on special order. In my hands and in those of my associate and the staff at Duke Hospital, this new instrument has been most satisfactory.

SUMMARY

A new female air cysto-urethroscope which was designed to combine the best features of the Kelly and Koch instruments and to avoid the undesirable features of both is presented. It is believed that this instrument provides better vision and greater usability for the urologist who uses the air cysto-urethroscope in a limited way than any instrument previously available.

This instrument may be obtained from V. Mueller and Company, Chicago
111 Broadway, Daytona Beach, Fla.

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vesicorectal anastomosis as described for the previous patient was performed. It should be noted that in this case, the anastomosis of the trigone to the anterior rectal wall provided adequate support for the rectum so that no recurrence of the prolapse was possible. The rectal sphincter soon regained its normal tone. After excision of the bladder the defect in the anterior abdominal wall was closed by approximation of the anterior sheaths of the recti muscles and migration of skin flaps. There was no postoperative urinary fistula or other complication and the patient was discharged on July 28.

The patient has had perfect urinary control through the use of her anal sphincter. She has attended school for the first time and cares for her own colostomy which has functioned with extreme satisfaction. There has been no fever or complaints of any kind that would indicate pyelonephritis or upper urinary tract infection. When last seen on March 13, 1952 cultures of the contents from the rectosigmoid bladder were sterile. Table 3 shows the blood electrolyte pattern since operation. It will be noted that here, as in case 1, there is no profound hyperchloremic acidosis which often follows ureteral transplantation. A tendency to hyperchloremic acidosis occurred only when the patient was on an acid ash diet as in experimental procedure (table 3). Figure 8 shows a typical postoperative excretory urogram, all of which have been entirely normal.

DISCUSSION

This or other operative procedures to anastomose the bladder to the rectum in order to employ the rectal sphincter for continence of urine in ectrophy of the bladder would seem more logical than ureteral implantation in which the long term results are uncertain and unproven. Ascending pyelonephritis or cicatricial obstruction of the terminal ureters in ectrophy of the bladder ordinarily does not occur before 5 to 7 years of age. In fact we have seen several individuals in their twenties and thirties with complete ectrophy of the bladder who showed an entirely normal upper urinary tract on excretory urography. Proper care of the patient and bladder up to the time of the operative procedure between the ages of 5 to 7 years should mitigate ascending urinary tract infection and anatomical changes in the terminal ureters at this age in life.

It is well known that malignant change may occur in ectrophy of the bladder either from a congenital predisposition or from long years in which there are infection and trauma to the exposed bladder. Trauma is the basis of the etiology in most likely. Of the 30 cases of malignancy reported in the literature as occurring in ectrophy of the bladder, 3 have been in the second decade in which the youngest was 23 years of age, 6 in the third decade, 10 in the fourth decade, 6 in the fifth decade and 5 in the sixth decade. The oldest of these was 66 years of age. There is no evidence therefore that nonexcision of the entire bladder before the ages of 5 to 7 would result in malignancy at a later date. The burden of proof would be on the author of a statement to the contrary. When malignancy in ectrophy is compared with the poor late results of transplantation, the mortality due to malignancy is far less than that due to transplantation and complete excision of the bladder. With sterile urine and the factor of irritation eliminated

siphon This flow of the fluid through the siphon tube creates a vacuum that aspirates the fluid of the bladder so that it remains empty The air, at the same time, enters in the needle (and you hear a little whistle), this air, resists the siphon effect and, once the bladder is empty, cancels it and the bladder is filled again In all cases each cycle of irrigation is adapted to the actual capacity of the bladder and the pressure remains always below 10 cm of water the height of the curvature of the siphon tube

Before starting the apparatus the air existent in its interior is evacuated for this purpose it is injected by the free extremity (outlet to waste) of the siphon tube with therapeutic fluid until it runs into the rubber tube connecting to bladder (close this extremity with forceps at its connection with the catheter) and arrives at the dropper (close it), afterwards it is connected at the catheter setting the dropper at 60 drops per minute So as to get acquainted with this apparatus it is recommended to connect the tube connecting with the bladder with a small rubber balloon making it function experimentally

When using the apparatus, the irrigating bottle that contains the therapeutic fluid must never be empty If it remains empty, the air will enter at the inside of the tube and it will be necessary to extract it

The parts necessary for building this apparatus are

A common irrigator (with one or two outlets, in case of using two outlets each, one of them carries a dropper and a connection in T thus permitting useful changes in the composition of the therapeutic fluid that washes the bladder)

A dropper (or two)

A connection of glass in T form of 4 mm of interior caliber (or metal (fig 1))

Three rubber tubes 1) A rubber tube of 140 cm length designed to connect the dropper with inferior arm of the T, 2) a rubber tube, approximately 80 cm in length designed to put in communication the horizontal arm of the T with the catheter (this tube is situated between the legs of the patient which warms up the therapeutic fluid), 3) a rubber tube of 100 cm length and 4 mm of interior caliber, designed to put in connection the superior arm of the T with the collector, this tube forms the siphon and is situated at the top of descending arm

A common needle of 0.2 mm of interior caliber

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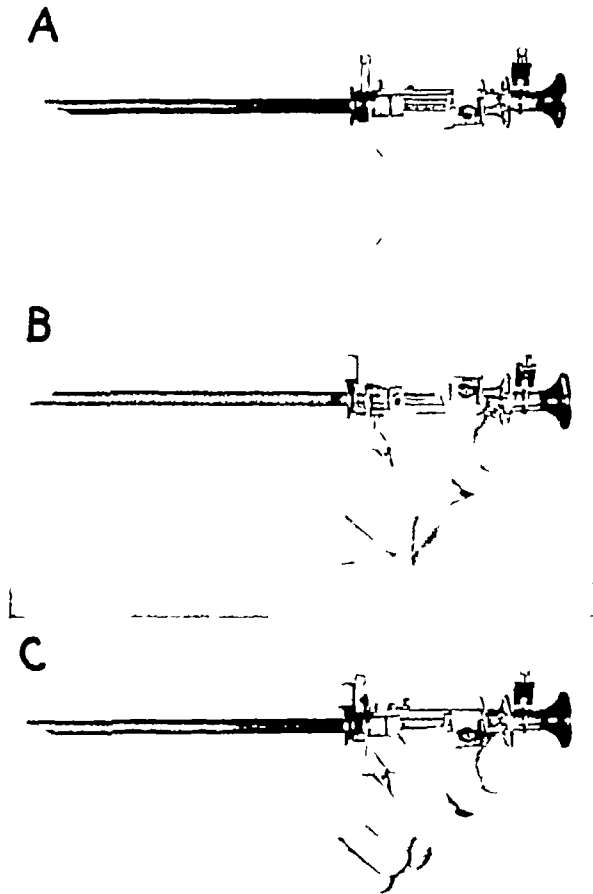


FIG. 24, handle and thumb rest attached to Berry sheath and original Nesbit working element. *B* assembled instrument in hand but with working element rotated to cut on roof of urethra. It will be noted that hand remains in same position with thumb under eyepiece and that water inlet remains on top. Hand remains in same position in all intermediate stages of rotation of working element with thumb under eyepiece in comfortable control of loop. *C* assembled instrument in hand with working element in position to cut on floor of urethra. Thumb is in position on plate of thumb rest.

ture yielded *B. coli* and *B. proteus*. Blood urea nitrogen and the 2-hour output of phenol-sulfonphthalein were normal. Excretory urography disclosed satisfactory renal function bilaterally, slight right hydronephrosis, normal left urinary tract, a trabeculated bladder, but an otherwise normal cystogram, no urinary calculi were visualized. Cystoscopy revealed 2 phosphatic calculi lying on the bladder floor, each stone measuring about 2.5 cm. in diameter. There was an intense chronic cystitis and slight intra-urethral enlargement of both lateral lobes of the prostate. There was no evidence of bladder tumor. Litholapaxy was performed followed in 4 days by transurethral resection of the prostate. Pathological report of the resected tissue was adenomatous overgrowth, with squamous metaplasia and chronic prostatitis. After this procedure the urinary symptoms subsided and the residual urine dropped to 60 cc, although pyuria continued and the urine remained alkaline in spite of antibiotics, sulfa drugs, and bladder irrigations with Subv. solution. However, the patient remained comfortable and free of urinary symptoms for the next 4 months.

In June 1950 painful and frequent urination again developed and the patient was re-admitted to the Jewish Hospital. On cystoscopy there was a severe cystitis, the vesical neck and entire roof of the bladder were covered by grayish-white, very adherent incrustations, giving the characteristic picture of alkaline incrustated cystitis. No tumor tissue could be seen. Excretory urography showed a mild degree of bilateral hydronephrosis with good renal function bilaterally. The cystogram was unsatisfactory. Residual urine measured 60 cc, it was alkaline in reaction and yielded *B. proteus* on culture. Antibiotics and sulfonamides were administered and the bladder was irrigated frequently with Subv. solution. This resulted in considerable improvement both subjectively and cystoscopically, the incrustations clearing completely from the vesical neck and diminishing on the bladder roof. After discharge from the hospital the patient remained fairly comfortable for about 2 months. Urinary difficulty then returned and was now accompanied for the first time by severe suprapubic pain and the development of 2 sinuses in the suprapubic area. Weakness and considerable loss of weight were also noted.

The patient was again admitted to the Jewish Hospital on August 12, 1950. His general appearance was poor. There was marked pallor and evidence of recent weight loss. Two small sinuses were present adjacent to the suprapubic operative scars; they drained small amounts of thin pus which was at times blood tinged. A smooth firm tender mass occupied the suprapubic region, extending from the symphysis to the umbilicus. It gave the impression of a distended bladder but on passage of a catheter which readily entered the bladder there was no residual urine and the mass remained unchanged. Rectal examination was negative. The temperature was 100 to 101 F. The urine was purulent and blood tinged. The hemoglobin was 67 per cent, the white blood count 20,900, with 79 per cent polymorphonuclears. The blood urea nitrogen was 26 mg. per cent. A diagnosis of prevesical abscess was made.

Operation was performed on August 14, 1950 under spinal anesthesia. A longitudinal suprapubic incision was made slightly to the right of the two old supra-

tissue. This is a very common sequela of an inadequate resection. The incidence of immediate and delayed hemorrhage in our patients has been found to be 3.32 per cent. Hemorrhage, although lowering the patient's physical reserve for the time being, does not often materially increase the period of morbidity.

Incontinence has occurred in 8.29 per cent of 500 consecutive cases, 7.02 per cent being temporary and 1.27 per cent permanent. None have had incontinence from open surgery with the exception of two patients with temporary incontinence from radical perineal prostatectomy. The prevention of incontinence is not to cut, unduly traumatize or fulgurate the external sphincter muscle. In open surgery the prostatic urethra must be carefully severed at the apex, never torn from the urethra.

Infection can cause considerable and prolonged distress when an incomplete operation, be it open or closed, has been performed. It has been our finding that an average period of 12.9 weeks elapses before the urine may be expected to clear after endoscopic resection. The principal causes of persistent infection are believed to be the result of not completely removing all of the hypertrophied tissue which becomes necrotic and hinders epithelization, or failure to eliminate any cause which might produce residual urine, such as stricture, diverticuli and detrusor decompensation.

Of 500 consecutive patients undergoing endoscopic prostatic resection urethral stricture has occurred in 16.17 per cent despite every precaution. Of these 60.5 per cent occurred at the meatus, 22.3 per cent in the mid-urethra and 23.6 per cent in the posterior urethra.

In approximately 75 to 80 per cent of our cases of endoscopic prostatic resections a postoperative elevation of temperature to 100 degrees or more developed. This appears to be an unusually high percentage but has occurred in spite of careful attention to asepsis both during and after the operation. It may possibly be explained that in carrying out much more complete removal of hypertrophied tissue than in previous years, with frequent opening into venous sinuses, bacteria and/or toxic material have much more ready access to the blood stream.

In an effort to reduce postoperative febrile reactions 100 patients undergoing endoscopic resections were administered prophylactic and postoperative antibiotics and compared with a control group who did not receive antibiotics prophylactically. Of those who received the prophylactic antibiotics, 78 per cent were febrile with temperature of 100°F or more and 22 per cent were relatively afebrile with temperature of 98.6 to 100°F. In the febrile group 38.46 per cent had temperature of 100 to 101°F, 29.48 per cent, 101 to 102°F, 19.23 per cent, 102 to 103°F, and 10.25 per cent, 103°F or more.

In the group which did not receive prophylactic antibiotics 77 per cent were febrile with temperature of 100°F or more and 23 per cent had temperature of 98.6 to 100°F. Of these, 35.06 per cent had temperature of 100 to 101°F, 31.16 per cent, 101 to 102°F, 12.98 per cent, 102 to 103°F, and 18.18 per cent, 103°F or more. There appears to be no great difference apparent in the two groups with one exception. In the group that received prophylactic antibiotics there was found a near 50 per cent decrease in the incidence of patients presenting a

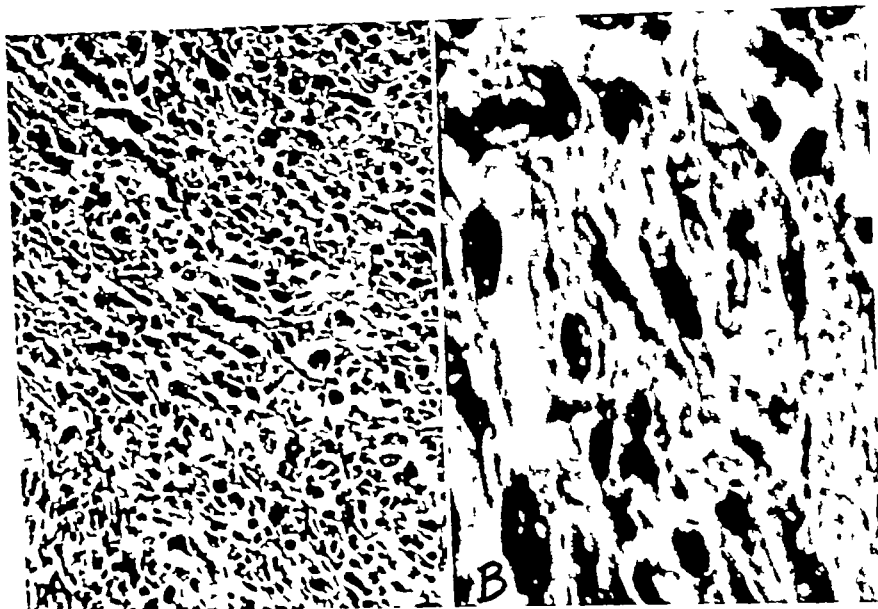


FIG. 1. A, leiomyosarcoma of bladder (hematoxylin and eosin, $\times 350$) B, leiomyosarcoma of bladder (hematoxylin and eosin $\times 500$), showing spindle shaped cells with large nuclei



FIG. 2. Autopsy specimen of opened bladder with attached ureters and kidneys also ureters invaded by tumor

in the prostatic fossa may produce incontinence by traumatizing the external sphincter and should not be ordinarily employed. Temporary urinary incontinence may occur, as described by Davis, in the absence of surgical injury to the sphincter muscle or its nerve supply. This is due to a preoperative disuse atrophy resulting from the obstructing prostate functioning as a barrier and the external sphincter being relieved of duty. Permanent incontinence is certainly ascribable to nerve and sphincter injury and may also be due to sensory and motor changes attributable to arachnoiditis secondary to spinal anesthesia.

The appropriate treatment for temporary incontinence is urethral dilations and sphincter exercises under direct supervision.

Pyuria, much to our surprise, has been found to persist for an average of 12.9 weeks. This figure was obtained by an analysis of prostatic resections from 1946 to 1949. During the past two years an effort has been made to reduce this complication by more complete resections and it is felt that a future analysis will be more encouraging.

Strict adherence to asepsis with closed drainage systems during and following surgery are practiced. Bladder irrigations are performed only to insure satisfactory drainage with the least amount of disturbance to the operative area. At times it may be necessary to disconnect the closed drainage system and irrigate with a hand aseptic syringe. Breaks in sterile technique are common at such times and proper instruction relating to bladder and urethral care are essential if infection is to be avoided. We agree with Buddington and Graves, that the mechanical introduction of bacteria is the most common source of bladder infection exhibited by patients who are on the conventional type of catheter drainage. All receptacles, tubing, and materials necessary for catheter drainage should be sterile and changed frequently. This is a very difficult problem to control since it is a nearly impossible task to convince attendants that bladder drainage is entitled to the same sterile techniques as demanded by open surgical wounds.

The prophylactic antibiotic practice does not appear to be indicated routinely, but we are inclined to concur with Merritt that it does seem logical to administer antibiotics, before and after endoscopic prostatic resections, to all patients who have a valvular heart disease. We have had the unfortunate experience of observing three fatal cases of bacterial endocarditis following endoscopic prostatic resection.

The postoperative prostatic patient is followed at two to three week intervals until the requirements for successful prostatic surgery are fulfilled.

When the operation of prostatectomy has been performed only a portion of the task has been accomplished and complete satisfaction, as to cure, is dependent to a large extent on careful and planned postoperative management. It has been our experience that endoscopic resection affords the patient suffering from obstructive prostatism a mortality of 1-30 per cent with an end result as satisfactory as with open prostatectomy.

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MUCINOUS CARCINOMA OF THE URACHUS INVADING THE BLADDER

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A total of 46 cases, besides our own, of mucinous carcinoma of the urachus invading the bladder have been described in the literature. The majority were men in the fourth and fifth decades. The youngest reported case was in a man 26 years of age.

REPORT OF CASE

H. I., a 52 year old Negro, was admitted to the Veterans Administration Hospital, North Little Rock, Arkansas, on June 3, 1949, with a diagnosis of psychosis manic depressive, mixed type. On June 9, 1949, he began to have frequency, nocturia and hematuria. Repeated urine examinations showed 30 to 35 red blood cells per high power field. Cystoscopic examination on June 14, 1949 showed a small, firm tumor with a hard base at the dome of the bladder. A diagnosis of malignancy was made. Because of the flatness of the mass, a satisfactory biopsy was not obtained. On June 29, 1949, cystoscopy was repeated. The tumor mass appeared about the same size as previously noted. Again a satisfactory biopsy was not obtained because of the flatness of the lesion. Suprapubic cystotomy and radium seed implantation into the tumor were recommended. On July 29, 1949 a midline incision was made and the bladder was exposed extraperitoneally. A mass about $3\frac{1}{2}$ inches in diameter was noted intimately attached to the bladder in the midline. The tumor was smooth and circumscribed and not adherent to the peritoneum nor attached to the umbilicus. It was surrounded by loose areolar tissue. There were no palpable lymph nodes. The upper one-third of the bladder together with the tumor mass was resected. Cut sections of the tumor mass showed it to contain a gelatinous material. It was not loculated or lobulated. The interior of the bladder showed a circular, sessile tumor, about $2\frac{1}{2}$ cm in diameter cauliflower in appearance, very hard and raised above the bladder mucosa about 1 cm. This tumor mass in the vault of the bladder was continuous with the above described cystic mass.

The entire specimen was hourglass in shape and measured 9 by 6 by 5 cm (fig. 1). The larger portion was oval and encapsulated. The wall here averaged less than 1 mm in thickness and was very fibrous. The contents of this large cystic mass were gelatinous and yellow gray, the material was tenacious and adherent to the cyst wall. There was direct continuity between the cystic mass and the portion of tumor involving the wall of the urinary bladder. The intravascular neoplasm was not encapsulated and extended into the vesical musculature. It measured 4 cm in diameter and was 2 cm thick. This mass was irregular, fungating and reddish gray. This tissue on cut section was firm and gray with areas of red brown softening.

Received in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Harrison⁷ reported that in 3 cases of malignant teratoma of the testis treated with bilateral orchiectomy and x-ray therapy there was no clinical evidence to the effect that removal of the sound testis played any role in improving the course of the disease. All of his patients received stilbestrol without benefit.

In 1945 Coutts and Vargas-Zalazar⁸ treated a case of seminoma and lumbo-aortic metastases with daily subcutaneous injections of progesterone and bilateral orchiectomy. There was remarkable improvement and reversal of a positive Friedman test.

In none of the cases in which improvement was noted on endocrine therapy was a definite mechanism of action postulated.

The following case is presented to illustrate the remarkable response of metastatic lesions of a seminoma, as manifested by pyelographic changes, to hormonal therapy.

CASE REPORT

A well developed, well nourished 34 year old white man was first seen on January 2, 1942 at the Atlantic City Hospital with an enlarged left testicle of 2 weeks' duration. The patient was an elevator operator and to his knowledge had been entirely well until 3 weeks previously when an elevator he was operating had fallen 17 floors. A physical examination immediately after the fall was entirely negative, but 4 days later he noted a gradually increasing, painless swelling of the left testicle accompanied by a drawing sensation in the left inguinal region. The patient had had an uncomplicated attack of gonorrhea 10 years previously, but there was no other history of urinary tract disease. The family history was unimportant.

Examination revealed a firm elastic mass in the left scrotum which conformed to the outline of the testicle. The surface was smooth and not attached to the skin. It was approximately twice the size of the right scrotal contents. The left testicle and epididymis could not be differentiated. There was nothing unusual within the abdomen. Neither kidney was palpable. Rectal examination revealed a smooth, elastic, movable prostate gland of normal size with no evidence of inflammatory changes. The seminal vesicles were not palpable.

On admission the red blood cell count was 5,100,000, hemoglobin 14 gm. and white cell count 6,800 with a normal differential count. A urinalysis was within normal limits. The Wassermann test was negative as was the Friedman test. X-rays of the chest, lumbar spine and pelvis showed no evidence of disease.

It was felt that the most likely diagnosis was orchitis and associated hematocele, with a malignant tumor as a possibility. Treatment consisting of the application of hot saturated solution of magnesium sulfate and elevation of the scrotum on an adhesive bridge was instituted. When no change was noted after eight days, a left orchiectomy was performed. The cord was ligated at the internal ring and removed with the left testicle. A Bassini repair was done.

Examination of the removed tissue revealed a testicle with a smooth capsule

Harrison, I. G. *Chimes* 3: 11, 1944.

⁸ Coutts, W. I. and Vargas-Zalazar, R. *Rev. Chilena de hig. y med. prev. (Santiago, Chile)* 7: 57-61, 1945.

The neoplasm is considered a mucinous adenocarcinoma of the urachus with invasion of the urinary bladder (fig. 2)

Suprapubic and prevesical drainage was carried out. All drains including the suprapubic drain were removed on August 5, 1949. On August 12, 1949, the suprapubic drain wound was healed and the patient was passing urine by urethra. The postoperative course was uneventful. The patient has been followed monthly since operation and up to this time (6 months' postoperative) has been symptom free without local recurrence or demonstrable metastasis.

DISCUSSION

These lesions are usually first seen by the urologist through the cystoscope. They may appear as ulcerated or papillomatous growths at the vault of the bladder. The symptomatology of this tumor is similar to other malignant tumors of the bladder. Often the first symptom is hematuria with frequency. Inflammatory phenomena may mask the hematuria since, as in all cases of cancer of the bladder, infection is likely to occur early. If infection is pronounced voiding is usually associated with pain. A low, tender, palpable mass in the suprapubic area and the voiding of mucilaginous material have been described in the literature.

When a lesion is visualized it is important that the character of the tumor be determined from a pathological standpoint. Proper treatment is directly dependent upon a correct diagnosis. This type of tumor rarely metastasizes before operation, but it has been noted that metastases are relatively frequent after operation. The consensus of all who have encountered this tumor is that radical surgical excision of the tumor is the only method of any value. Some have advocated removal of the peritoneum over the bladder together with the umbilicus. The accepted therapy of papillary tumors of the bladder such as fulguration or radium seed implantation is valueless in urachal tumors. The latter contention is based on the fact that the lesion visible through the cystoscope is no criterion of the actual size of the urachal neoplasm since the bulk of the growth is intra-abdominal and erosion through the bladder is a late manifestation.

In the case presented satisfactory biopsy was not obtained and because of this fact the true nature of the tumor was not suspected until operation. This case again emphasizes the importance of thorough examination in all cases of hematuria.

SUMMARY

A case of carcinoma of the urachus invading the bladder has been presented. The clinical diagnostic and therapeutic features of this tumor have been reviewed.

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were palpable. There was moderate tenderness on fist percussion at the left costovertebral angle. The right scrotal contents were not unusual. The findings on rectal examination were identical with those of the first admission.

X-ray examination on his second admission failed to reveal evidence of metastases to the chest or dorsal spine. A plain film of the abdomen was noncontributory. Excretory urography revealed prompt excretion of the contrast medium on the right side with a normal right upper urinary tract. There was no appearance of dye in the left kidney even on a delayed film.

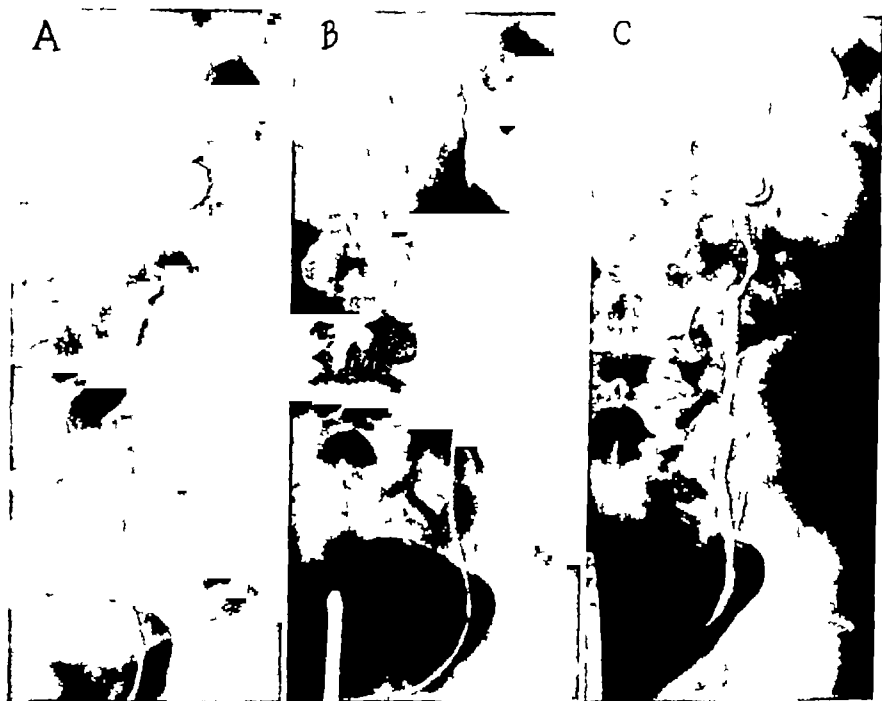


FIG. 2. *A*, left retrograde pyeloureterogram, dorsal position. Shows marked hydronephrosis with obstruction at and below ureteropelvic junction due to metastases involving para-aortic nodes, irregularity of lumbar ureter. *B*, left retrograde pyelogram, dorsal position, after one month of estrogen therapy. Renal pelvis is normal in size and contour. *C*, left retrograde pyeloureterogram, dorsal position, 1 month after discontinuing diethylstilbestrol therapy. Reveals recurrence of hydronephrosis with irregularity of upper ureter due to external pressure.

The red blood cell count at this time was 3,500,000, hemoglobin 10 gm. The white blood cell count was 8,200 with a normal differential. The urine was normal. The blood urea nitrogen was 11 mg. per cent. The Friedman test was positive. The serum acid phosphatase was not elevated.

Shortly after admission a right orchiectomy was performed. After an uneventful recovery the patient was subject to cystoscopy to elucidate the left upper quadrant mass. Examination of the bladder, vesical neck and posterior urethra was entirely within normal limits. A 5F ureteral catheter was inserted 30 cm up the left ureter without encountering obstruction. Retrograde pyelography (fig. 2, *A*) revealed a marked left hydronephrosis with obstruction of the ureter

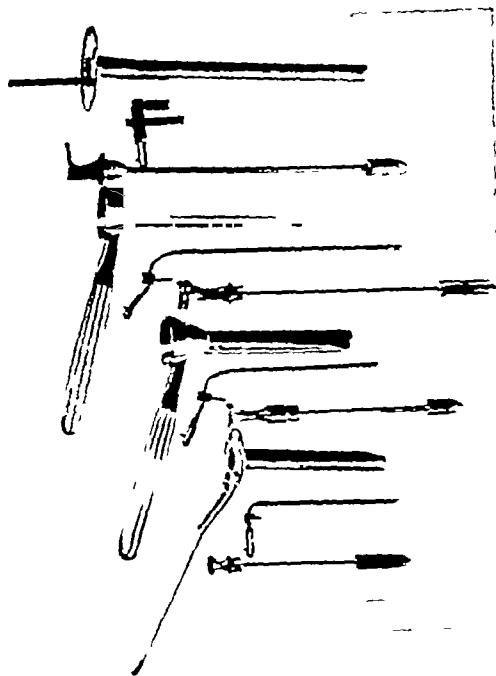


FIG. 1 From top to bottom relative sizes, light source, and obturators are shown of the Young male urethroscope, Kelly female urethroscopy cystoscope, Goddard female urethroscopy cystoscope, and Koch female urethroscopy cystoscope. Note the Kelly female instrument is nearly as long as the Young male instrument. Also note the undesirable flat surface which the Koch presents to the operator. The handle on the Koch instrument was made in our shop and is not standard equipment.

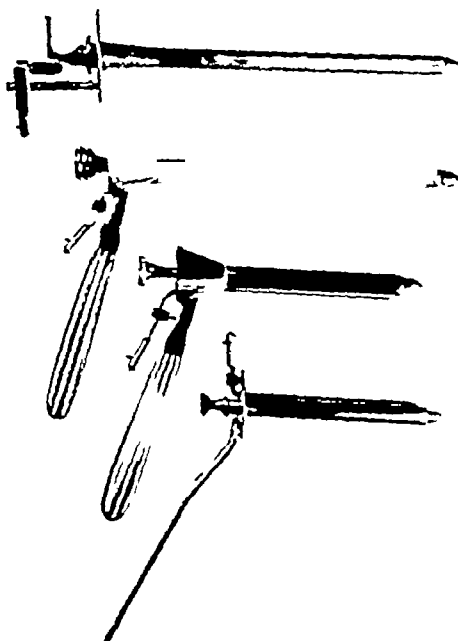


FIG. 2 Assembled instruments shown in figure 1 in same order.

suggests that we may biologically modify the soil to inhibit the growth of malignant cells. To hypothesize the mechanism by which this is accomplished, we may profit from reconsideration of information gained in the study of carcinoma of the prostate. Dean and others¹⁰ have found that 45 per cent of cases of carcinoma of the prostate show as much or more androgen content in the urine after castration as previously. This has been interpreted to mean that castration often results in compensatory production of androgen by the adrenal glands, and that this extra gonadal source of androgen may explain the failures in treatment of carcinoma of the prostate by this method. It has also been shown that 66 per cent of cases have an increase in serum gonadotropic hormones after castration, indicating a stimulation of the pituitary gland. No such increase is noted after estrogen therapy.

One possible explanation in our case is that the benefit resulted from a neutralization of adrenal androgen by diethylstilbestrol. Although removal of the second testicle did not result in apparent improvement, this procedure 13 days prior to the institution of stilbestrol therapy may have facilitated this neutralization. The recurrence of this man's tumor might have been delayed for a much longer period of time had he not discontinued his estrogen therapy.

While the result in our case was most striking, we realize that one case is of little value and that a large series will be required to establish the worth of this type of therapy in inoperable metastatic testicular carcinoma. We hope that the recent renewed interest in adrenal physiology will, in the near future, clarify the possible role of the adrenal androgens in the etiology of carcinoma of the testicle and carcinoma of the genito-urinary tract in general.

SUMMARY

The literature concerning the role of endocrine therapy in carcinoma of the testis with metastases has been reviewed.

A case of seminoma demonstrating the regression of metastatic lesions is evidenced by changes in psychographic findings in response to estrogen therapy has been reported.

A hypothetical discussion as permitted by our present knowledge is presented.

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¹⁰ Dean, A. I., Woodward, H. R. and Twombly, G. H. *J. Urol.*, **49**, 105, 1943.

AUTOMATIC TIDAL DRAINAGE APPARATUS

FRANCISCO MARTINO SAVINO

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By means of this apparatus we can obtain an endless irrigation of the bladder, the bladder is filled slowly with the therapeutic fluid and also with the urine that arrives from the kidneys, being emptied quickly when the pressure increases up to 10 cm. of water. This cycle is repeated indefinitely.

I describe here in easy way to build one of these devices by means of a common irrigator and a glass tube connection in T form. The apparatus is shown in figure 1.

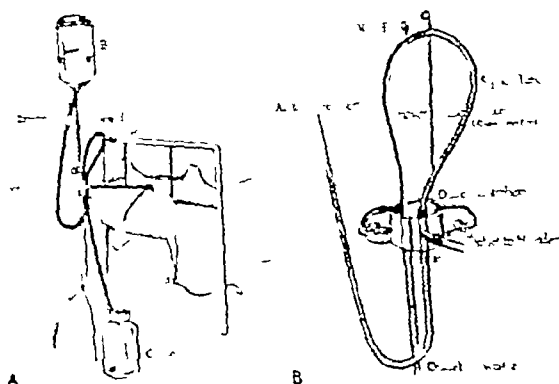


FIG. 1

The irrigator is situated at the foot of the patient's bed. The irrigating bottle is connected at the dropper (rhythm 60 drops per minute). The connection in T (glass tube of 4 mm.) is fixed with elastoplast at the support of the irrigator at the same level of the patient's pelvis as is shown in figure 1. The dropper is connected at the lower end (inlet) of the connection in T. The horizontal arm of this connection (outlet to bladder) is connected by means of a rubber tube, to the bladder and the superior one to a rubber tube of 4 millimeters the other end of which is attached to the collector (outlet to waste) placed on the floor below the bed of the patient. This rubber tube forms the siphon and its curvature should not be more than 10 or 15 cm.

In the top of the descending arm of the siphon is situated a common injection needle of 0.2 mm. This needle is designed to allow the entrance of air on the inside of the siphon tube.

Use of the apparatus: The therapeutic fluid passes from the irrigating bottle to the dropper arriving at the lower arm of the connection in T (inlet) and, owing to gravity, passes to the horizontal tube (outlet to bladder) connecting to the bladder. When the bladder is filled the therapeutic fluid flows by the superior arm of the connection in T, passes by the ascending arm of the siphon tube, runs through its curvature and goes out by the descending arm of the

temic effect when introduced into the peritoneum. With these known facts, it was thought advisable to note the action of Solusponge *in vitro* and *in vivo*.

Because Solusponge seemed to present rapid solution in body fluids we decided to try this hemostatic sponge in various urological procedures. Particularly in the prostate, where it would be so easy to increase the urinary amylase in case vestiges of the starch should remain, this substance proved to be a safe, nontoxic hemostatic agent that could be left in the body. In addition, it presented certain physical properties with many advantages over the absorbable hemostatic sponges.

This substance was studied *in vivo* and *in vitro*. The results showed that this substance was innocuous.

Following prostatectomy, and the packing of the cavity with this agent, the substance was completely eliminated in 72 hours. There were no untoward reactions.

Due to the lack of space allowed, description of cases and details are omitted. Therefore, our conclusions are as follows:

DISCUSSION

We have taken specimens from the drainage of some of these patients 24, 48 and 72 hours after operation and have examined them under the microscope in an effort to ascertain something about the time element involved in the digestion of the starch. There are numerous starch granules seen as late as 48 hours postoperatively. However, after 72 hours the urine is clear and there are no granules present, both on inspection under the microscope and also after adding Lugol's solution.

That amylase, the starch enzyme, would hasten the digestion of the Solusponge is known, however, having determined the fact that normally the material is practically eliminated after 48 hours, there is no need, nor is it desirable, to have this substance removed sooner. This is a nontoxic material as shown by investigators seeking an innocuous powder for sterile operating gloves. They proved starch, when dusted into the peritoneal cavity, caused no ill effects and was completely absorbed.

With this communication we are presenting an innocuous digestible material for hemostasis, especially suitable to prostatic surgery.

This research was carried on through funds furnished by H. L. Kreilsheimer. Solusponge furnished by the Pinray Corporation.

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MODIFICATION OF NESBIT RESECTOSCOPE

HUGO E. MILLER

The many modifications of the Stern-McCarthy electrotome indicate a dissatisfaction with the existing equipment. The instrument presented herewith is a modification of the original Nesbit single bar working element and the Berry rotating inlet sheath. The common difficulty with this working element was the inability to make the block and loop perform smoothly. The original thumb rest was removed and the one pictured substituted. The thumb rest is a plate and ring so made that the telescope runs through the center of each. The loop is advanced by pressure on the plate and, if necessary, assisted on the return by pressure with the back of the thumb on the ring. (See figs. 1 and 2)



FIG. 1. Handle and thumb rest shown separately.

The handle is made to fit the rotating collar of the Berry rotating inlet sheath and is held in place by the snugness of the fit. The handle is bent so that a firm, comfortable hold can be had with the instrument in the working position at the eye.

In operation, with the handle stationary, the working element and sheath can be rotated completely with the water inlet remaining stationary. The plate and ring of the thumb rest keep the same relation to the telescope throughout rotation and the thumb remains in the same comfortable position under the eyepiece in complete control of the loop. The instrument is completely controlled by one hand, leaving the other free for the manipulation of the prostate through the rectum. It is impossible to exert pressure on the thumb rest other than parallel to the line of motion of the block and the block and loop run freely. Binding due to bending of the sheath is reduced because the finger in the rectum makes it easier to engage the tissue in the loop by pressure on the prostate and during extreme angulation of the sheath less necessary.

The thumb rest has been in use since 1946 and the handle on the Berry sheath since 1949.

blood loss in the group of patients on which he has reported? Has the urine become blood-free in a shorter interval than in patients in whom the sponge has not been used?

Finally I would like to compliment Dr Ritter for his extensive laboratory and clinical investigation of this new material

DR J SIDNEY RITTER The starch, as we all know, absorbs liquids. It swells, and exerts immediate compression of venous system. We do arrest active arterial bleeding where indicated.

I agree with Dr MacDonald in the point that we should attempt arresting active bleeding wherever possible. We have not measured the blood loss in any of our cases, but, we were forcibly impressed with the fact that postoperatively, the day following surgery, there was practically no macroscopic blood to be found.

POST-OPERATIVE TREATMENT FOLLOWING PROSTATIC SURGERY

JAMES B. GLANTON, LOUIS M. ORR AND JOSEPH C. HAYWARD

In recent years, before the advent of endoscopic prostatic resection, the operation of prostatectomy was considered one of the greatest of surgical hazards. The mortality rate varied between 10 and 20 per cent. The period of morbidity involved many months with oftentimes permanent disabling consequences.

With improved surgical techniques and with increasing appreciation of the necessity for preoperative preparation, the mortality rate for open prostatectomy is at present between 3 and 6 per cent and endoscopic prostatic resection between 1 and 2 per cent. Associated with this better understanding of the causes of death from prostatectomy has been the development of antibiotics. These drugs must be given their proper importance in the reduction of both the mortality and morbidity rate.

Despite the fact that the death rate from prostatic surgery is now on a satisfactorily comparable basis with other forms of surgery, it would seem prudent, at this time, to give attention to those measures which are essential in the reduction of morbidity.

In 1000 consecutive patients with obstructing prostatism endoscopic prostatic resection was the operation of choice in 94.33 per cent, suprapubic prostatectomy in 3.25 per cent, perineal prostatectomy in 1.37 per cent, and retropubic prostatectomy in 1.05 per cent. The average amount of tissue removed by endoscopic resection was 24.5 g. This discussion will, therefore, principally concern morbidity as related to endoscopic resection, but those patients undergoing open prostatic surgery must also be carefully observed in order to prevent those same unfortunate sequelae which may follow endoscopic surgery. In our experience, however, open prostatic surgery is followed by a lessened morbidity.

In any form of prostatic surgery the requirements which must be met in order to give the patient a satisfactory result are 1) that he be able to void freely, not too frequently, and empty his bladder, this implies that no small caliber urethral stricture be present; 2) that his urine be free from infection, and 3) that complete control be retained.

To translate satisfaction of these requirements into terms of precautionary measures to be taken to lower morbidity entails a discussion of postoperative complications, both immediate and remote. The four principal complications are 1) hemorrhage, 2) incontinence, 3) continuing pyuria and 4) urethral stricture. Any or all of these may follow or be associated with prostatic surgery.

Hemorrhage may be classified as immediate, delayed and recurrent. Immediate hemorrhage may occur within one half to several hours following surgery and is due to failure to control bleeding adequately in the operating room. Delayed hemorrhage usually occurs within the first two to three weeks and is due to physical exertion, trauma and unknown factors. Recurrent hematuria is a delayed type of bleeding that occurs intermittently over months and even years, resulting from necrosis of the irregular portions of the remaining prostatic

¹ Lecturer in Urology, Southern Section, American Urological Association, Memphis, Tenn., March 1951.

enable one to arrive at the correct diffusible calcium value. Abnormal total serum calcium values may be misleading unless this finding is correlated with that of total serum protein. This is of aid in arriving at the diagnosis of hyperparathyroidism. The Sulkowitch test of the urine may be used as a quick simple office procedure for screening patients and selecting those to be subjected to the expense of blood chemical determinations for further study.

PHOSPHORUS

The serum phosphorus level has a definite clinical significance in these studies. Phosphorus metabolism is influenced by the parathyroid glands. It is believed that the essential action of the parathyroid hormone is to lower the renal threshold for phosphates, presumably by inhibiting the reabsorption of these substances in the kidney tubules. Thus, overactivity of these glands as in hyperparathyroidism is associated with increased phosphorus excretion by the kidney and decrease in serum phosphorus level. In hypoparathyroidism the reverse circumstance prevails. In states of renal insufficiency the serum phosphorus is elevated.

PHOSPHATASE

The term phosphatase is used to designate an enzyme which may be measured in the circulating blood serum. The phosphatase activity measures, in arbitrary units, the ability of this enzyme to decompose a pure, known amount of phosphate ester under controlled conditions of time, temperature, and pH. If the reaction is carried out under acid conditions the result is a measure of the *acid phosphatase activity* of the serum, if the reaction is carried out in an alkaline medium the result is a measure of the *alkaline phosphatase activity* of the serum.

The alkaline phosphatase is believed to be produced by the osteoblasts or bone forming cells. It is absorbed by the lymphatics and the blood stream. Its excretion is by way of the biliary system. Therefore in the absence of obstructive jaundice, an elevation of the serum alkaline phosphatase is an indication of increased bone formation. In the presence of Paget's disease of the bone it may be elevated as much as forty times its normal reading, though in an early localized Paget's there may be no significant elevation of this enzyme. It may also be elevated in the presence of osteoblastic type of metastatic carcinoma, and in 100 per cent of cases of hyperparathyroidism with bone involvement.

The serum acid phosphatase is produced by the tissues of the prostate gland. The ability to produce acid phosphatase in large amounts is retained by prostatic carcinoma. This enzyme apparently does not enter the blood stream in any significant clinical amounts except in extension of carcinoma of the prostate through the prostatic capsule. It has been found to be elevated in 85 per cent of the cases of carcinoma of the prostate with demonstrable metastases. It is not elevated in any significant clinical amounts in any other disease. The fate of this enzyme in the body has not been clearly established.

The following diseases have been chosen for discussion. The most important data on each are presented in the accompanying charts.

temperature of 103°F or more. The routine use of prophylactic antibiotics has been discontinued.

The postoperative care following prostatectomy deals primarily with the preventive measures related to the complications encountered. The end result following prostatic surgery is in direct proportion to the effectiveness and completeness of the postoperative management.

In an effort to reduce the incidence of delayed hemorrhage we have compiled a brief but specific list of instructions (Do's and Don'ts) for the patient. This deals principally with restrictions to reduce any physical activity which might produce bleeding. Driving of automobiles, climbing stairs or lifting heavy objects is prohibited for a period of three to four weeks.

Approximately two to three weeks postoperatively the anterior urethra is carefully calibrated with sounds and steel olive-tipped bougies. Gentleness must be strictly adhered to since new areas of urethral fibrosis may be caused by forceful instrumentation. Five to six weeks following surgery when healing has usually progressed satisfactorily the entire urethra is calibrated and any evidence of stricture is appropriately managed by regular progressive dilations.

Prostatic massage is not indicated if complete adenectomy has been performed and massage of this region would not appear to be conducive to healing. Delayed hemorrhage might be precipitated by this procedure.

In endoscopic prostatic resection as in all forms of surgery, gentle handling of tissue is a prerequisite to normal healing. The mucous membrane of the urethra is extremely sensitive to trauma and fibrous tissue diathesis should be considered a variable factor in wound healing. Stricture oftentimes occurs when least suspected. To avoid stricture which is one of the most frequent and discouraging complications, resectoscopes of the proper size must be utilized. Meatotomy and perineal urethrotomy are performed when the slightest urethral snugness is evident. What may appear to be very minimal trauma can be the responsible factor in ischemia of the urethral mucous membrane with a resultant disabling stricture. In this group of patients meatotomies were done in 18.29 per cent and perineal urethrotomies in 4.46 per cent. In recent months these procedures and smaller resectoscopes have been used more frequently and we believe the end results will be more gratifying by noting a definite decrease in the incidence of stricture. By using a Charrière scale it is surprising to note that the so-called 28F resectoscope with metal covered sheath measures actually 30F and the 28F Thompson resectoscope measures 32F. The adult male urethra will not in many instances, admit these so-called 28F instruments without causing considerable trauma. The 26F resectoscope with metal covered sheath, actually measures 26F on the scale.

The silver-treated catheter as recommended by Ockerblad is used during the immediate post-operative course. It is believed that this catheter produces less urethral traction and a lessened incidence of stricture. The catheter is usually removed 72 hours following surgery since prolonged urethral catheter drainage may in itself be prejudicial to normal healing.

Incontinence is to be avoided by very careful resection and fulguration of the urethra and the external sphincter muscle. It is believed that traction on catheters

TABLE 5 *Metastatic Thyroid, breast, kidney, lung*

KUB	OTHER BONES	BLOOD CHEMISTRY				GENERAL
		Phos tase		Ca	P	
		Acid	Alk			
Osteolytic lesions	Spine or long bones	N	N*	N	N	History phys Exam Pneulogram chest film Search for pri mary source
Localized or gen eral Kidney shadow				High in rapid bone destr		

* Increased in rare osteoblastic lesions

TABLE 6 *Metastatic Carcinoma of prostate*

KUB	OTHER BONES	BLOOD CHEMISTRY				LUNG
		Phosphatase		Ca	P	
		Acid	Alkaline			
Localized or diffuse lesions	Skull to rule out Paget	High in 85% cases with bone metas	N May be elevated in predom os teoblastic lesions	N	N	Very rare except in assoc with other metas
Osteoblastic or osteolytic						
Pelvis, vertebra, ribs (late)						

TABLE 7 *Important findings*

	F.C.B.	BLOOD CHEMISTRY				BLOOD PROTEINS	URINE	BONE MARROW	GENERAL
		Phosphatase		Ca	P				
		Acid	Alk						
Senile osteoporosis	General decalcific								
Hypoparathyroid ism	Renal calcinosis or calculus			High	Low		Increased calcium excre tion		
Paget's	Fibro-cystic changes		High						Skull and tibia
	Local general								
Multiple myeloma	Small punched out lesions					Total high A/G Ratio reversed	Bence Jones protein	Myeloma cells	
Metastatic Thy roid Breast Kid ney Lung	Lesions osteolytic or osteoblastic								Search for pri mary
Metastatic Ca Prostate	Lesion osteo blastic and or osteolytic	High							Rectal examina tion

apparently a failure of osteoblastic activity. Thus, one would not expect any significant changes in the blood chemistry. There may be some increase in the urinary calcium excretion in the early stages of the disease. See table 1.

CLINICAL EFFECT OF ESTROGEN THERAPY ON METASTATIC LESIONS FROM CARCINOMA OF TESTIS

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From the Department of Urology, Atlantic City Hospital, Atlantic City, N. J.

The urologist's interest in the endocrinological treatment of malignancy has been markedly stimulated in recent years by the response of prostatic carcinoma to orchiectomy and estrogen therapy. Consequently, the influence of estrogens upon advanced malignant disease of many types has been studied with generally disappointing results.¹ Nevertheless, reports by the senior author² and Lich and Grant³ of the symptomatic benefit afforded sufferers of advanced bladder carcinoma by castration and endocrine therapy have nurtured the hope of discovery of a more general relationship between the sex hormones and tumors of the urogenital tract.

The relationship of hormones to testicular tumors has been thoroughly studied by Twombly and others.⁴ In addition to the effect of estrogen on testicular tumor, Twombly has investigated the effect of antigonadotropic sera in patients with testicular tumors and large amounts of chorionic gonadotropin in the urine, without success in either instance. In 1942, J. C. McClelland,⁵ in discussing a paper before the American Urological Association, reported on a patient with embryonal carcinoma of the testicle and generalized metastases who, after removal of the remaining testicle, improved, with disappearance of the metastases as evidenced by palpation and x-rays of the epigastrium and lungs. The involved testicle was removed in April 1941. In September 1941, roentgenograms showed metastases to the lungs. In October 1941, there was a palpable mass in the epigastrium. At this time the remaining testicle was removed. Two months later the epigastric mass could not be palpated and 3 months later no roentgen evidence of metastases remained. The patient's general condition gradually improved and he was last seen 1 year later, at which time he was apparently well. No roentgen therapy was given after the second operation, although he had received three courses of high voltage roentgen therapy prior to October 1941.

Sedley,⁶ in August 1942, performed a bilateral orchiectomy on a 50 year old man with a teratoma of the left testicle and a metastatic mass occupying the epigastrium. From August to September 1942, the patient received radiation therapy to the extent of 3500r in fractionated dosage. This patient's general condition improved and the epigastric mass could not be palpated by November 1942. There was a marked weight increase and in October 1943, the physical examination was negative and no evidence of recurrence was detected. The Friedman test, which was positive prior to orchiectomy, became negative.

Presented at annual meeting American Medical Association, Atlantic City, N. J., June 13, 1943.

¹ H. H. A. Watkins, I. and Paterson, I. British Med. J., 2, 393, 1944.

² Sedley, C. H. Det. J. Urol. 54, 539, 1945.

³ Lich, J. S., Jr. and Grant, O. J. Urol. 59, 682-686, 1948.

⁴ Twombly, C. H. Surgery, 16, 181-193, 1944.

⁵ McClelland, J. C. In discussion of article by Davis, I. J. Urol., 49, 14 (p. 31), 1943.

⁶ Sedley, C. H. Det. J. Urol. 119, 262, 1944.

changes, urinary tract disease, and hypercalcemia. In many cases no bone lesions are present. When bone changes are present they consist of generalized decalcification, with superimposed cysts or tumors, i.e. osteitis fibrosa cystica. There is an increase in both the osteoblasts and osteoclasts in these lesions. There is



FIG 3 1, advanced Paget's disease of bone. Increased thickness and heavy appearance of bones, due to osteoblastic activity and subperiosteal ossification. Fibrocystic areas. B, moderately advanced Paget's disease. Typical bony changes throughout left side of pelvis. Bony trabeculations in ilium adjacent to hip joint. C, early Paget's disease. Thickening of cortex and fibrocystic changes in left ilium. Bony trabeculations

an absence of the lamina dura around the teeth. The skull may have a ground glass appearance in addition to cysts. The urinary tract lesions may be nephrocalcinosis or one or more kidney stones. Bilateral diffuse calcification in the renal parenchyma may be due to other causes, however, the persistence of a high serum calcium and a low serum phosphorus is diagnostic of hyperparathyroidism. The urinary calculi seen in the stage prior to secondary bacterial invasion are of the calcium oxalate or the calcium phosphate variety. The most constant chemical findings are hypercalcemia, hypophosphatemia, and hypercloturia.

On section there was a loss of normal structure and it consisted of a mass of soft yellow tissue with hemorrhagic mottling. Microscopic examination (fig 1) revealed a fibrous stroma enclosing broad sheets of uniform cells. The cells were large and ovoid with a rim of clear cytoplasm. The nuclei were round, the chromatin fine grained and a nucleolus prominent and centrally placed. The connective tissue septa were infiltrated with occasional lymphocytes but there were no focal collections of these cells. When this tissue was first examined a diagnosis of embryonal carcinoma was made but a recent restudy of the slides leads us to believe that it represents a seminoma.

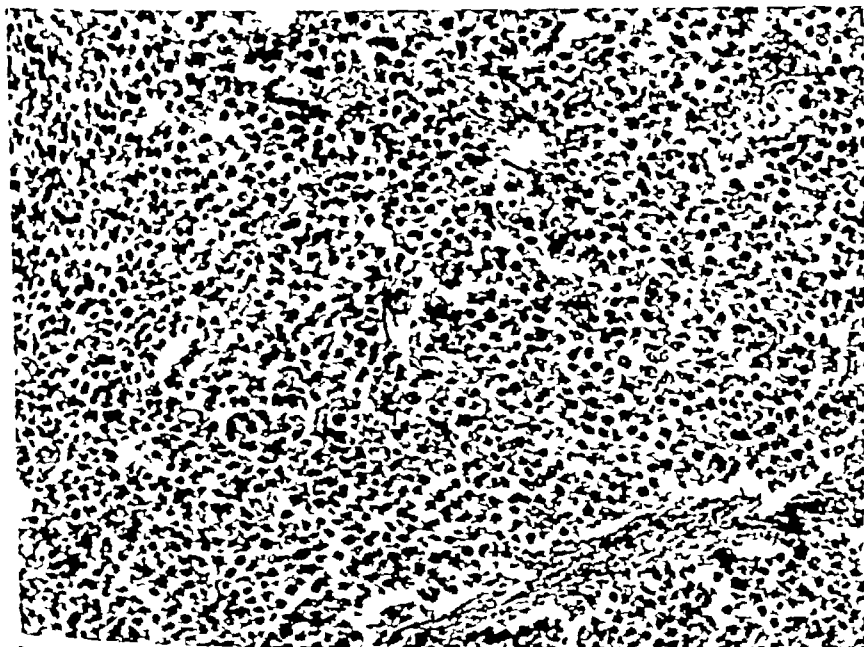


FIG. 1. Left testicle. Photomicrograph shows tumor composed of masses of large, uniform, rounded polyhedral cells with relative clear cytoplasm. Nuclei are round, chromatin fine grained and a nucleolus prominent and centrally placed.

The patient was discharged on February 21, 1942, with instructions to report to the Outpatient Department for a course of x-ray therapy. He received 3000 rads of x-ray dose over a 3 month period following his discharge but then refused to submit to further x-ray therapy. He was next seen at the Atlantic City Hospital 7 months after the cessation of his x-ray therapy when he complained of a dull constant ache in the left flank of several months' duration and a mild swelling in the epigastrium for a short time. He also noted a constant ache in the left scapula for the past 6 weeks and there had been a 35 pound weight loss during the preceding month.

Examination at this time revealed a cachectic individual. The inguinal nodes were well headed. There were bilateral palpable movable inguinal nodes. There was a firm fixed nontender mass occupying the left upper quadrant of the abdomen, attached to the skin. No other abdominal masses or organs

fibrous tissue some of which degenerates leading to cysts, thus, the term "fibrocystic" is applied to the appearance of the bone. Irregular trabeculations of bone are present. There are cases in which deficient calcification and abnormal structure are apparent and this results in deformities due to relative lack of rigidity in the bony skeleton. This disease is of particular interest to the urologist because it produces bone lesions which are most likely to be confused with metastatic carcinoma of the prostate. Distinguishing features of Paget's, however, in addition to the appearance of the bone lesions in the plain urogram are typical skull involvement, sabre shin, normal acid phosphatase, and very high serum alkaline phosphate. See table 3.

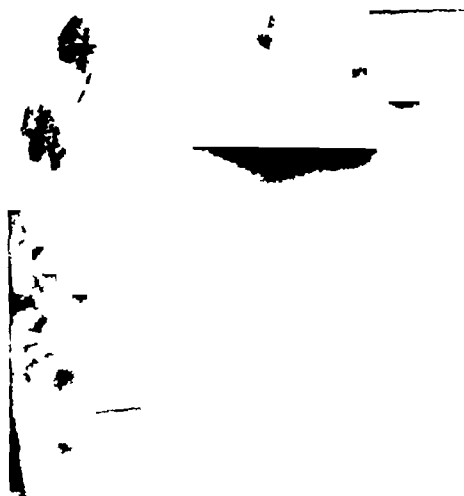


FIG 6 Carcinoma of kidney. Destructive osteolytic process localized to one lumbar vertebra.

MULTIPLE MYELOMA

Bone lesions in this disease can vary but the typical case presents small punched-out osteolytic areas. Ribs, spine, pelvis, and skull are commonly involved. Much confirmatory evidence is available where the bone lesions suggest multiple myeloma, namely, urine findings including the Bence Jones protein, bone marrow studies hyperproteinemia with reversal of the A-G ratio due to increased blood globulin. Therefore, since approximately one half of blood calcium is combined with the proteins, total blood calcium determinations will in many cases be above normal. Blood phosphorus will ordinarily be found normal except in terminal cases where renal insufficiency and consequent retention of phosphorus occurs. See table 4.

METASTATIC CARCINOMA OF THYROID, BREAST, KIDNEY, AND LUNG

These lesions arise principally from the sites enumerated. Hans F. W. Lither in 1948 analysed a series of 470 cases of carcinoma which had metastasized to bone.

at and below the ureteropelvic junction. It was concluded that these changes were due to metastases involving the para-aortic glands with extrinsic pressure on the upper ureter.

During the 2 week period following the removal of his remaining testis, there was no noticeable improvement in the left upper quadrant mass. It was then decided to administer estrogen in the form of diethylstilbestrol. He was given 10 mg intramuscularly daily for a period of 5 days when the dose was reduced to 5 mg daily because of nausea and vomiting. After 9 days of therapy it was noted on ward rounds that the left upper quadrant mass was significantly smaller in size. Three days later the left upper quadrant mass was soft, smooth, indefinite in outline and at least 75 per cent decreased in size.

After 1 month of the therapy, a retrograde study (fig 2 B) of the left upper urinary tract was carried out. In marked contrast to the original study, the renal pelvis and calyces approached the normal in size and contour and renal function as evaluated by indigo carmine excretion was excellent bilaterally. At this time the left upper quadrant mass was not palpable on physical examination and the patient was discharged from the hospital with instructions to take 5 mg of diethylstilbestrol orally daily. One month later when the patient who was irresponsible and of low mentality reported back to the clinic he advised us that he had failed to take any of the prescribed medication. A retrograde pyelogram (fig 2 C) now showed a recurrence of the left hydronephrosis with irregularity of the left upper ureter. A Friedman test was positive. This was the last time the patient was seen at the Atlantic City Hospital. Subsequently it was learned that from April to August 1943, the patient received x-ray therapy to the extent of a total of 2600 air r. to each of four anterior abdominal ports at the Philadelphia General Hospital. No further follow-up is available from that institution.

Thus during the month which elapsed between the first and second pyelograms at the Atlantic City Hospital the only treatment carried out was the administration of either 5 or 10 mg diethylstilbestrol intramuscularly daily. Clinically there was marked regression of the mass within 9 days of the institution of stilbestrol therapy. The removal of the sound testicle had been carried out 12 days prior to the first pyelogram and 13 days before the institution of diethylstilbestrol therapy. The patient had received no x-ray therapy for at least 7 months prior to his second hospital admission. That the metastatic lesion was not prostatic in origin is assured by the location of the metastases, the benignancy of the prostate on rectal examination and the normal values of the serum acid phosphatase.

DISCUSSION

With endocrine therapy has not been generally recognized as a factor in the management of testicular tumors, a review of the literature reveals an inadequate response to this type of treatment in enough cases to demand further evaluation of the relationship. However, any attempted explanation of the complexity of the interrelation of sex hormones to carcinoma must remain hypothetical in the light of our present limitation of knowledge. Herbert

ance The sites of metastasis may be seen in the spine and pelvis and also in other bones There are no characteristic changes in the blood chemistry, except in cases of rapid and widespread bone destruction which may result in a high blood calcium To be emphasized in the diagnosis of these conditions is a thorough clinical history and a general physical examination Pyelograms and x-rays of the chest will be of value in the search for the primary source See table 5

METASTATIC CARCINOMA OF PROSTATE

This is the bone lesion most often seen by the urologist in the plain urogram It is the bone lesion in which he is most interested and which he must differentiate as positively as possible from all others In contrast to most other metastatic bone lesions, metastatic carcinoma of the prostate is predominately osteoblastic though mixed-type lesions are seen, and rarely pure osteolytic changes occur Pelvis, spine, and ribs are usually involved in that order The most valuable confirmatory finding in suspected metastatic carcinoma of the prostate is elevation of the serum acid phosphatase It is increased in 85 per cent of cases with bone metastasis Alkaline phosphatase is increased in proportion to the amount of osteoblastic activity Lung metastases are very rare except in association with other metastases A solitary metastatic lesion in the lung, without evidence of other metastases, is practically never due to carcinoma of the prostate See tables 6 and 7, and figures 1 to 7

CONCLUSIONS

An attempt has been made to condense and tabulate the pertinent data on bone changes in cases in which the urologist most frequently sees in his daily study of the plain urogram The presentation consists of 1) elementary but fundamental considerations needed in the interpretation of bone lesions, 2) discussion and tabulation in condensed form of the classic features of some bone lesions in which the urologist is most interested, and 3) suggestions as to additional clinical, laboratory and x-ray data which are of value in proving or disproving a diagnosis of a presenting bone lesion, and 4) illustrative x-ray films

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SOLUSPONGE AS A HEMOSTATIC AGENT IN UROLOGY

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In urology the surgeon is confronted with two major complications: infection and hemorrhage. With the advent of antibiotic therapy the former has been reduced to a minimum; the latter has now taken over the major role of disaster. This is especially true in surgery directed toward the relief of prostatism.

During the past few years many and varied local and systemic coagulants have been advocated for hemostasis. These have not changed the problem.

From time to time many systemic coagulants have been used. But these were of little effect unless the individual on whom they were used had a basic deficiency. Furthermore, while it is desirable to bring blood coagulation time to normal, it is not advisable to increase the coagulability of the blood in individuals undergoing surgical procedures because of the increased dangers of thrombophlebitis.

A moment's pause to state that in patients showing signs of emboli following prostatic surgery, vena cava ligation is the only means of satisfactorily combating this serious complication.

It became customary to use packing made of gauze or some other material which had to be removed from the prostatic bed. This controlled the immediate situation only; the possibility of secondary hemorrhage resulting from pulling away some of the fibrinous coating with the gauze remained.

With the introduction of materials that could be left in the body in the form of a sponge that would disintegrate slowly, great expectations were held by urologists. But these absorbible sponges proved to be dangerous in certain cases because they left a residue in the prostatic bed which had to be removed, some of these surgically. Irrigations with suitable solutions as indicated to remove these substances are essential; however, this active procedure caused mechanical contractions of the bladder and activated the sphincters which on many occasions resulted in early removal of clots and active hemorrhage. In some cases small amounts of material left in the region of the prostate remained as nidus for calculus formation. Furthermore, many of these agents were local irritants and caused vesical and urethral spasms followed by prolonged periods of urinary retention and tenesmus.

With the hope of effectively finding a coagulant, or better still a mechanical agent, for arresting bleeding and at the same time finding one that could be eliminated from the bladder automatically by simple solution, digestion or absorption through the good graces of Dr. A. I. Lichtman, our attention was called to Solusponge. This substance is an acrated starch. Starch is a drying agent; for sterile gloves has been advocated and is used freely today. It is found to be easily digestible and absorbible, leaving no unfavorable local or sys-

whether they are located within the Golgi apparatus,¹⁵ the centrioles, the reticulum or bodies of the cytoplasm or nucleoplasm,¹⁵ the myelin of neurons, myofibrils of muscle fiber, and fiber of flagellum, or cells of the hormone producing glands of the testis,* corpus luteum, placenta or adrenal cortex, etc.^{4 6 7 8 16}

Evaluatively, sudan black B is unsuitable for differential staining of specific lipids.^{4 6 7 8 16} Any mild differential staining theoretically available is technically lost in the composite color resulting from the mixture of lipids almost invariably present in organelles and lipid-containing food reserves.^{5 9} Conclusively, notwithstanding the lack of differential lipophilic staining of sudan black B, it nevertheless remains invaluable in contemporary lipid cytochemical studies.

MATERIALS, TECHNIQUES AND PROCEDURES

The cell source for this study is man.¹⁷ The spermia obtained as ejaculate¹⁸ were spread as a film and fixed in Schaudinn's fixing fluid (saturated aqueous HgCl_2 (66 cc), 95 per cent ethyl alcohol (33 cc), and glacial acetic acid (1 cc) added at time of use). Testicular autopsy or biopsy frozen sections provided material for tissue study.

After thorough washing (aqueous), the cell films or sections were immersed in (staining jar), or else covered (wet cover-slip preparation) with sudan black B stain. This stain was prepared by adding to saturation sudan black B powder in 70 per cent ethyl alcohol. This mixture was allowed to stand 24 hours or longer before using, thereby assuring solution and consequently largely preventing confusing undissolved particles of stain from entering into the microscopic field and cell picture. The stain in solution may precipitate out on standing and require filtering. Immersed slides should be and were tilted with cell side down in the staining jar thereby using gravity to further prevent precipitated-dye¹⁹ particles from adhering to the cells. The cells were exposed to the stain for 30 minutes (heated) to 24 hours (room temperature) and rinsed in 70 per cent ethyl alcohol before recorded observations or drawings were made.¹⁹ Wet cover-slip preparations necessitated repeated additions of stain solution or alcohol (70 per cent) in order to prevent drying of the specimen cells while under observation. Colorless Karo served well as mounting media for semi-permanent slides.† Oil immersion objective and 20 X ocular were used in making the camera lucida drawings (fig. 1).

* Observe that the sterol producing cells of the testis (interstitial) are functionally endocrine and are not associated directly with spermatogenesis.

¹⁵ Baker, J. R. The structure and chemical composition of the Golgi element. *Quart J. Micro. Sc.* 85: 1, 1945.

¹⁶ Wislocki, G. B., Dean, H. W. and Dempsey, F. W. The histochemistry of the rodent's placenta. *Am. J. Anat.* 78: 281, 1946.

¹⁷ Brown, R. I. On the care of human sperm. *J. Lab. & Clin. Med.* 29: 211, 1944.

¹⁸ Brown, R. I. Some environmental factors which effect the life span of human spermatozoa. *Urol. & Cutan. Rev.* 49: 336, 1945.

¹⁹ Brown, R. I. Sudan black B in male fertility studies. (In press.)

† Either transparent Karo or a viscid, aqueous or weak alcoholic (ethyl) solution of sucrose (boiled) may be used as mounting media in the preparation of semipermanent mounts. The cover slip may be if desired sealed (gold seal, etc.) for greater permanency. Slides thus prepared have shown no deterioration or other changes after two years without any storage precaution.

DISCUSSION

DR S A MACDONALD (Montreal, Canada) Dr Ritter has brought to our attention new material that may prove to be of great value. It seems to possess some desirable characteristics, which have been lacking in other hemostatic substances previously available.

The complete solubility of this new sponge is probably its most important attribute. It is in this respect that it differs most from the gelatin sponge on which I had the honor to report to this society several years ago. Further experience with that sponge showed that due to its lack of solubility, it could cause complete retention during the patient's convalescence.

The rate of disintegration of this new Solusponge is of great clinical importance. Its liquefaction will be governed in general by the factors which determine the solution of starches. Its breakdown might be delayed by a low urinary pH or a diminution or absence of chloride ions from the urine. The presence of these ions is essential to enzyme activity. On the other hand, the premature disappearance of the sponge might give rise to secondary hemorrhage.

Dr Ritter has suggested that the hydrolyzing enzymes are derived from the urine and the blood. Another possible source of enzyme is from the bacteria which may be present in the bladder. Many bacterial strains produce abundant quantities of amylase. Active proliferation of such organisms probably will be produced by the rich sugar medium resulting from the hydrolysis of the starch.

Apart from its solubility another advantage of this new material is that it is not derived from any human source. This fact is important because, as a result, it will not be likely to transmit any viral infection. Cases of viral hepatitis are beginning to appear following prostatectomy. In these cases the source of infection has been traced to hemostatic substances of human origin.

A third advantage of the Solusponge is that, unlike previous materials, it does have an innate hemostatic quality. This characteristic is due to breakdown of sugar products which are released in high concentration on its surface. Such concentrated sugar solutions cause agglutination of red corpuscles, and thus facilitate blood clotting.

The main hemostatic action, however, of all sponge-like materials is due to their great surface area composed of innumerable cell-like spaces which they expose to the shed blood.

Furthermore they are compressible and allow the prostatic fossa to contract. In these two respects they would seem to be superior to oxidized gauze and inflatable bags.

In conclusion, probably it can be said that arterial bleeding following prostatectomy cannot be controlled adequately by any of the presently available hemostatic agents. After removal of the gland major bleeding points should be ligated. Following such ligation further hemostatic measures may not be necessary.

I would like to ask Dr Ritter if it has been possible for him to measure the

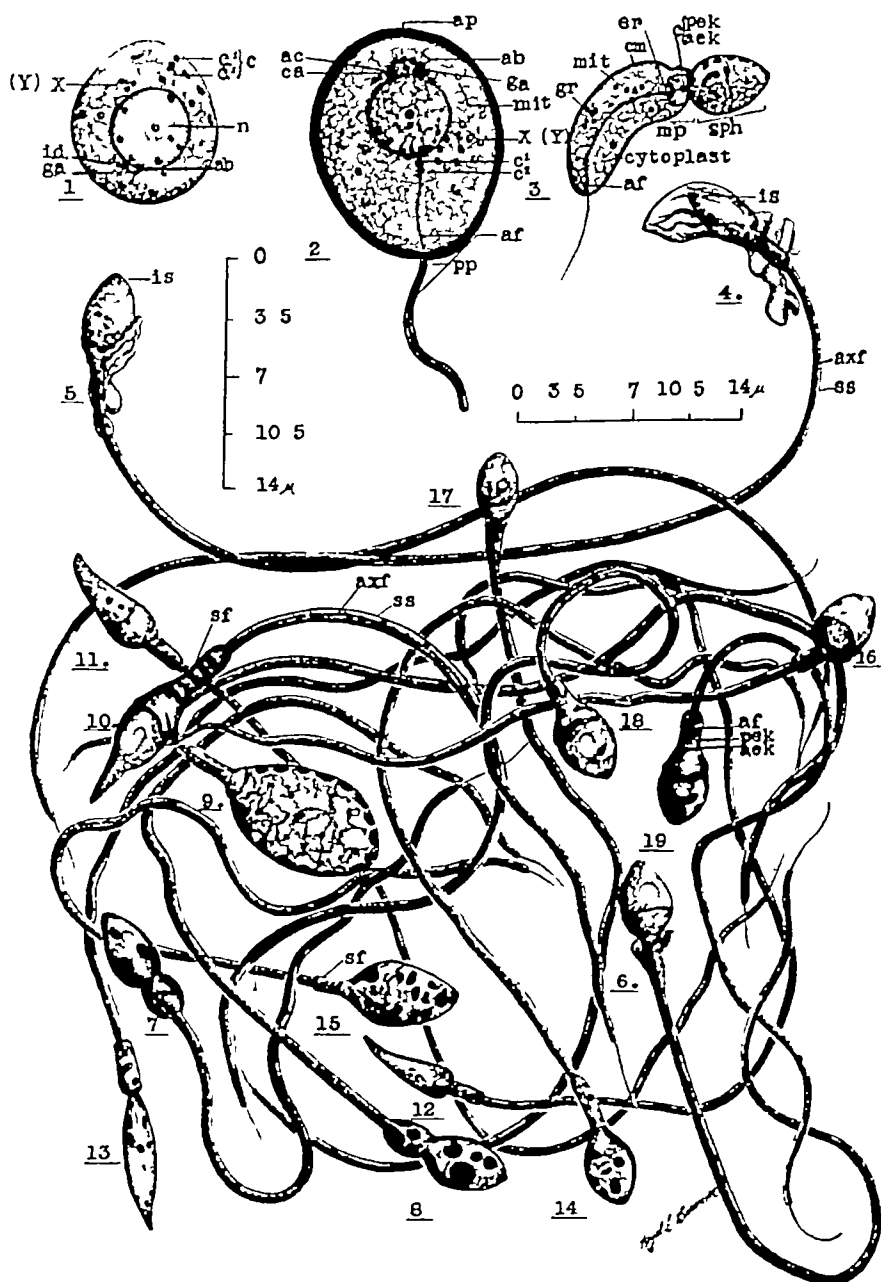


FIG. 1. Lipid distribution in spermatogenic cells (1-3) and peria (4-19) as determined by lipophilic sudan black B. All drawings were outlined by camera lucida and completed in detail.

sudan black B it appears that the previously included centrioles (c, fig. 1, 1), leave the karyosome (id) where they have fun in close proximity to the nuclear

INTERESTING BONE CHANGES IN PLAIN UROGRAMS

W. L. FITZGERALD AND M. D. THOMAS, JR.

In urological practice patients frequently are seen with the primary complaint of pain in the back, thighs, or limited to the right or left side of the abdomen. These patients may or may not have urinary symptoms associated with these pains. In an investigation of these cases the urologist is often the first physician to use recourse to an x-ray as a diagnostic aid in evaluating these complaints. Thus the plain urogram may reveal the first evidences of the existence of pathological processes in the bone. It is the purpose of this presentation to give in a condensed manner a) some of the more important fundamental considerations prerequisite to proper identification of bone lesions, b) the classic appearance of some of these lesions as the urologist sees them, and c) the most important additional data which may be needed to substantiate the clinical diagnosis of such lesions. Due to the multiplicity of causes of bone lesions only those will be discussed which, in our opinion, are of the most interest to the urologist or most commonly seen by him. No thought will be given to primary bone tumors, inflammatory diseases of the bones, or the various types of arthritis. Brevity likewise demands the exclusion of renal rickets and the now rarely seen osteomalacia. It is not within the scope of this discussion to enter into the minute diagnostic procedures which at times may be needed for a definitive diagnosis. The use of consultations with radiologist, orthopedist, and internist will be desirable in many cases.

BONE METABOLISM

Bone is a living tissue, bone metabolism is a continuous, active process simultaneously involving osteoblastic and osteolytic activity, also deposition and absorption of calcium salts. The metabolic rate however, as compared with other body tissues is very low. Some bone lesions are predominately osteoblastic while others are osteolytic. The fact that both processes occur side by side and simultaneously explains why mixed-type lesions are sometimes seen in the same disease. Metastatic carcinoma of the prostate and Paget's disease frequently present mixed type lesions.

CALCIUM

The calcium of the body is contained largely in the skeletal system with smaller amounts in the tissues and the circulating blood. Calcium is absorbed in the small bowel, it is excreted in the small bowel and the urine. Variation in calcium metabolism will cause variations in the amount of urinary calcium. The blood calcium is composed of both a nondiffusible and a diffusible or ionized calcium. The nondiffusible calcium is bound to the blood protein, and constitutes approximately 50 per cent of the total calcium of the blood. The diffusible calcium is the physiologically active calcium. If the total serum protein and calcium values are known use of the McEwen-Hastings chart will

presumably formed from the anterior division of the posterior centriole.¹⁴ The axial fiber of the flagellum is observed to be in some instances morphologically adjoined to and continuous with this *posterior end knob* in sudan black B preparations (fig 1, 9, 12, 17, 19). The end ring (er) which forms from the posterior centriole, presumably its posterior part, shows well when stained with sudan black B (fig 1, 4-19).

The *mitochondria*, many units of which are lost in the metamorphosing processes,³ particularly by way of the released mass of cytoplasm (fig 1, 3) maintains representation in the mature spermium by reforming into the *spiral fiber* (sf) of the *middle piece* (mp) (2-4 μ). However, most of the mitochondrial elements do remain in the discarded cytoplasm as it extends posteriorly (fig 1, 3) along the axial fiber and remains attached for some time *in toto* or in part to the *middle piece*. Some units or fragments may remain along the axial fiber of the mature spermium flagellum (fig 1, 4-19).

In figure 1, 3, the sudan black B staining organelles and structures are the nuclear membrane and cell membranes (cm) e.g., cell wall and plasma membrane and the nuclear and cytoplasmic granules, e.g., mitochondria (mit), Golgi (gr) centrioles (c), and their derivatives, i.e., the anterior (rek) and posterior end knobs (pek), the end ring (er), and the axial fiber (af and rxf). All derivatives of the centrioles, mitochondria, and Golgi apparatus have stained blue-black without exception. The mitochondria of the middle piece (sf) have not developed into a spiral configuration but appear as isolated bodies, oval or elongate. The so-called spiral filament in most mature spermia does not show a continuous spiral with sudan black B (fig 1, 4-19). In fact, only in few instances is there a semblance of a spiral structure, and, when present, it appears applied internal to the outside membrane of the middle piece, rather than the perfect mechanical spiral frequently illustrated within the cylindrical middle piece. The end ring (er) and the axial fiber are conspicuous in figure 1, 3, as they invariably are with sudan black B. Within the nuclear portion of the head, several oval blue-black bodies are in evidence. Their significance remains enigmatic. The line of demarcation between the acrosome and the nucleus is apparent. The acrosome similarly contains peripherally located granules, particularly in its very apex, but is otherwise essentially transparent. These sudan black B staining granules (fig 1, 3-19) retained by the apical tip of the head are believed to constitute an organelle derived from the mitochondrion or Golgi apparatus. It, though not previously described in human spermia, is probably homologous to the *perforatorium* observed in insects.^{20, 21} That it does not serve as a mechanical perforator but apparently acts chemically and enzymatically to impregnate the ovum has suggested the term *impregnasome* (is).¹⁴

In figure 1, 4, 5, and 6, amorphic portions of the cytoplasm particularly the cell wall portion, remain attached to the middle piece.^{11, 12, 14} These fragments usually contain little or no stained internal cytological structures, the cell wall

¹⁴ Bowen, R. H. On the acrosome of the animal sperm. *Anat. Rec.* 28: 1, 1921.

¹⁵ Bowen, R. H. On a possible relation between the Golgi apparatus and secretory products. *Am. J. Anat.*, 33: 197, 1921.

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TABLE 1 *Senile osteoporosis*

KUB	AGE	OTHER BONES	BLOOD CHEMISTRY			
			Phos tase		Ca	P
			Acid	Alk.		
General decalcification	Advanced years	Same as KUB	N	N	N	N

TABLE 2 *Hyperparathyroidism*

KUB	OTHER BONES	BLOOD CHEMISTRY				URINE
		Phos tase		Ca	P	
		Acid	Alk.			
Renal calcinosis or calculus	Localized cystic changes Large bone swellings	N	N*	High	Low	Increased Ca excretion†

* Increased 100% of cases with bone changes

† Sulkowitch test

TABLE 3 *Paget's (osteitis deformans)*

KUB	AGE	SKULL, OTHER BONES	BLOOD CHEMISTRY			
			Phos tase		Ca	P
			Acid	Alk.		
Localized or general fibro-cystic changes Pelvis and vertebra Trabeculations	Mid life to advanced years	Thickening of skull Moth-eaten Sabre shin	N	Very high	N	N

TABLE 4 *Multiple myeloma*

KUB	OTHER BONES	BLOOD CHEMISTRY				BLOOD COUNT	BONE MARROW	URINE	
		Phosphatase		Ca	P				Blood Protein
		Acid	Alk.						
Same as KUB	Same as KUB	N	N to high	N to very high	N	Elevated in 50%	Atypical white cell	Findings of Nephritis	
				High in 50%		A/C Ratio reversed G ⁺ tubulin elevated	Progressive Hypochromic anemia	Bence-Jones Protein (60%)	

SENILE OSTEOPOROSIS

This condition is not uncommon. The plain urogram will show uniform decalcification of the bones of the vertebrae and the pelvis. It is said to less frequently affect the skull or the extremities. The basic pathological change is

derivatives, are likewise observed to be blue-black following exposure to sudan black B, generally accredited to be a trustworthy lipophilic stain

These results would indicate that lipids are conclusively an intrinsic part of most if not all of the important organelles of the spermium. Evidently, therefore, lipids in one or more of their various forms and relationships, chemically and morphologically, and presumably physiologically, enter into the activity and reactivity of the spermium which performs most of the vital cell functions in addition to its major function in fertilizing the human ovum.

In this respect, it is further observed that the apex of the acrosome of the mature spermium head contains stainable lipids.¹⁴ That this structure and probable organelle serves physicochemically in the impregnation processes seems likely.

It is further observed that the many diagrams which illustrate a regular spiral thread encased in a cylindrical middle piece (body) are excessively mechanical in their implications, and, although more accurate than the preformation-theory illustrations of the spermatist, nevertheless, these frequently depicted interpretations do over-emphasize and exaggerate the antiquated mechanical explanation and neglect a truly physiochemical interpretation of the nature of this portion of the spermium.

SUMMARY

Sudan black B stained slides indicate that most of the kinetically important cellular structures of the spermatogenesis series of cells contain lipids.

Organelles which stain blue-black are the mitochondria, the Golgi apparatus, the centrioles, the acroblast, axial fiber, end ring, spiral filament, anterior and posterior end knobs, and granules (impregnasome) in the apex of the mature head. The cell wall, membrane, and nuclear membrane also stain blue black, and, in some instances are thicker than previously indicated by iron hematoxylin stains. The ground protoplasm of the cytoplasm and nucleus contains barely discernible particles which are dispersed within the meshwork, giving it color when stained with sudan black B. The cytoplasm and nucleoplasm also contain blue-black condensation particles, some of which may be unrecognized organelles.

It is believed that the lipids of these functionally important structures actually enter chemically and physiologically into the vital process assumed by these important structures, including a role in the impregnation process of the ovum wall.

A stained series of spermia and their spermatogenic antecedents indicate the metamorphic changes which have progressively occurred among spermatocytogenic and spermiogenic cells. Furthermore, the stained histological elements are sufficiently diversified as to make this technique valuable in evaluating spermia morphologically in fertility studies.

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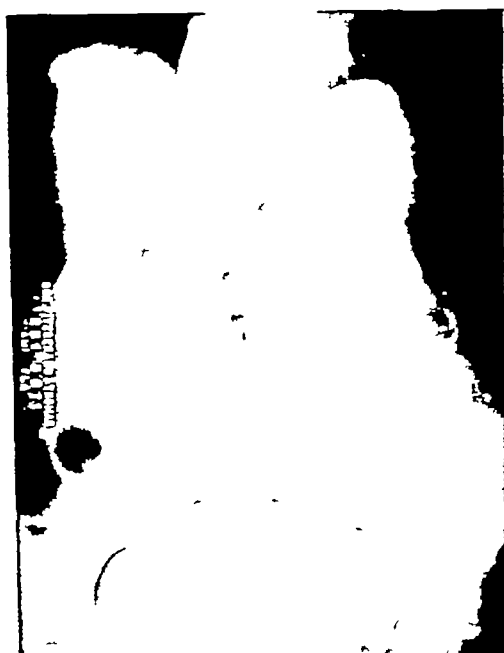


FIG. 1. Senile osteoporosis. Appearance of generalized bony decalcification.



FIG. 2. *A*, hyperparathyroidism. Renal calcinosis. No bone changes. Consistently high blood phosphorus. *B*, hyperparathyroidism. Unilateral renal calcification. Osteitis fibrosa cystica.

HYPERPARATHYROIDISM

Hyperparathyroidism is caused by overactivity of the parathyroid gland due to adenoma or hyperplastic parathyroid tissue. The clinical findings are due to the bone

calyces are atypically arranged, depending on the nature of the mal-rotation, and may point inward toward the spinal column, or downward, or both. The ureters enter the pelvis higher up than in nonfused kidneys, arising from the inner border of the upper part of each kidney and passing over the anterior surface of the renal mass.

In over 90 per cent of cases the isthmus consists of renal parenchyma of considerable breadth and thickness, but it may be merely a thin, fibrous union. Usually the isthmus lies in front of the aorta and vena cava, very rarely behind them, and, according to Young, still more rarely between them. The kidney is generally fixed by its isthmus to the surrounding structures and vessels at the level of the third or fourth lumbar vertebra.

There is great variation in the origin, number, and size of the arteries supplying each renal mass, as well as in the veins. As is common with all displaced kidneys, the vessels may arise from the nearest great vessels and this fact must be borne in mind when operating upon the horseshoe kidney. Arterial branches from the inferior mesenteric, common iliac, and external and internal iliac arteries commonly supply the fused kidney, in addition to those from the aorta.

The diagnosis is made by urography. Excretory urograms will usually establish the diagnosis, unless there is serious destruction of parenchyma, but retrograde pyelograms are preferable. The pathological horseshoe kidney, especially if it contains stones, can sometimes be recognized in a plain film.

GROUPING OF CASES IN RELATION TO TREATMENT

Regarding the management of horseshoe kidney, three things must be borne in mind: 1) Horseshoe kidneys may exist without producing symptoms. 2) Most symptoms are caused by secondary renal disease rather than by the fusion. 3) Much less frequently, a horseshoe kidney without secondary pathological changes may, by reason of its anomalous state alone, produce symptoms demanding relief.

Group 1: Horseshoe kidneys with no renal abnormality other than fusion and no symptoms due to the anomaly. This is the most common type, and is discovered accidentally at autopsy or during routine examination (pyelography). Surgery is not indicated, though it is advisable for such individuals to be observed from time to time.

Group 2: Horseshoe kidneys with secondary renal lesions, with or without symptoms referable to the kidney. This is the most common form of horseshoe kidney diagnosed clinically. Hydronephrosis, infection, and calculus are the most frequent lesions, with tuberculosis relatively common, and rarer instances of polycystic disease, solitary cyst, pyonephrosis, nephritis, tumor (including Wilms' tumor), and trauma. Hypertension may result from unilateral disease of a horseshoe kidney and be cured by renal surgery.

The frequency of secondary lesions is due to several factors: 1) the unusual position and curvature of the ureters, due to their abnormal insertion and course, resulting in pressure upon them; 2) the regularly anomalous vessels, which predispose to obstruction of the ureters by direct pressure; 3) fixation of the fused kidney by its isthmus to the surrounding structures and vessels, resulting in kink

The serum alkaline phosphatase is elevated only in cases with bone involvement
See table 2



FIG. 4. *A* skull in Paget's disease. Moth-eaten appearance. Thickening of skull plate
B Paget's disease. Sabre shin

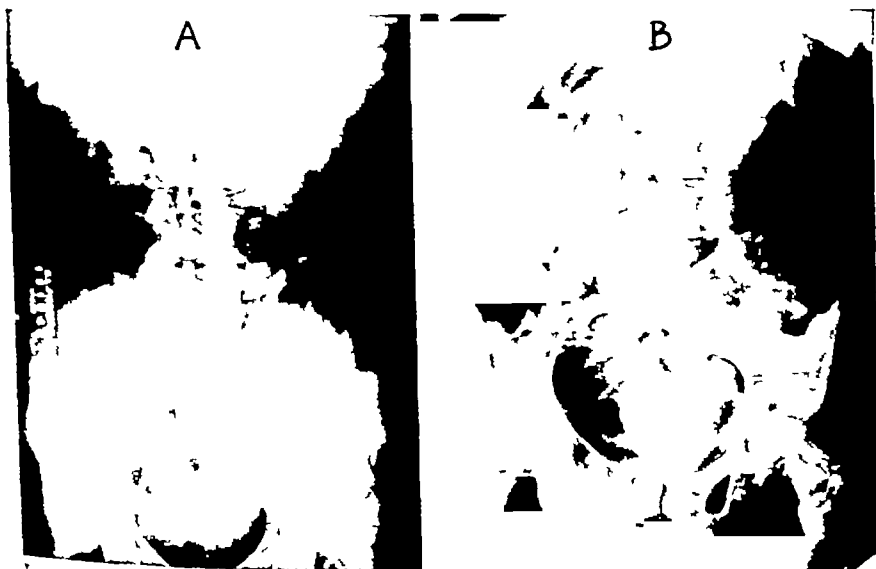


FIG. 5. *A* multiple myeloma. Typical punched out osteolytic lesions of left skull base, process 13 and twelfth rib left. *B* carcinoma of breast. Wide-spread osteolytic lesions. Film made 5 years following radical amputation of breast

PAGET'S DISEASE OF BONE

This disease is characterized by simultaneous osteolytic and osteoblastic lesions, both of which are increased in tempo. The cortex of the bone exhibits osteoporosis and thickening. Portions of the bone structure are replaced by

For many years, the author has utilized the following operation in horseshoe kidneys with hydronephrosis and infection, with excellent results. The operation consists in 1) division of the isthmus, 2) ureteropelvioplasty, or dilatation of the ureter by a splinting catheter brought out through a nephrostomy wound, as indicated, and 3) elevation of the kidney by nephropexy.

Technique The patient is placed on his side, with the loin on the stretch, and fixed in position with two strips of adhesive plaster.

An incision is made from the costovertebral angle downward and inward for about 18 to 20 cm. This is deepened through the subcutaneous fascia and muscular layers, care being taken to preserve the lower branch of the twelfth subcostal nerve and also the ilio-inguinal and iliohypogastric nerves. Gerota's fascia is opened and the kidney mobilized carefully, the numerous aberrant vessels always encountered being ligated before being cut.



FIG. 1. Preoperative radiogram showing tremendous hydronephrosis of right half of horseshoe kidney and slight hydronephrosis of left half (Same patient as figures 2 to 9).

The isthmus is isolated, and two rows of ribbon-gut sutures are placed in position on either side of the contemplated line of division. The isthmus is then divided between them, the sutures being utilized to hold in place pieces of fat applied to the cut edges to control hemorrhage, which sometimes may be quite brisk.

After division of the isthmus, the kidney on the side of the loin incision is pulled over laterally. If, as is usually the case, there is considerable hydronephrosis due to obstruction at the ureteropelvic junction, a small incision is made in the renal pelvis to determine if there is narrowing due to actual stricture. Through this a splinting catheter is introduced into the narrowed ureter (a Foley Y-plate being done on the ureteropelvic junction if necessary). The pelvis is drained with a Malecot catheter, both catheters being brought out through a nephrostomy wound which is closed with a pad of fat held in place by ribbon gut, if this is necessary to secure hemostasis.

Carcinoma of the breast led the list with 47 per cent exhibiting bone metastases. Then followed, in order, carcinoma of prostate 42 per cent, thyroid 30 per cent,

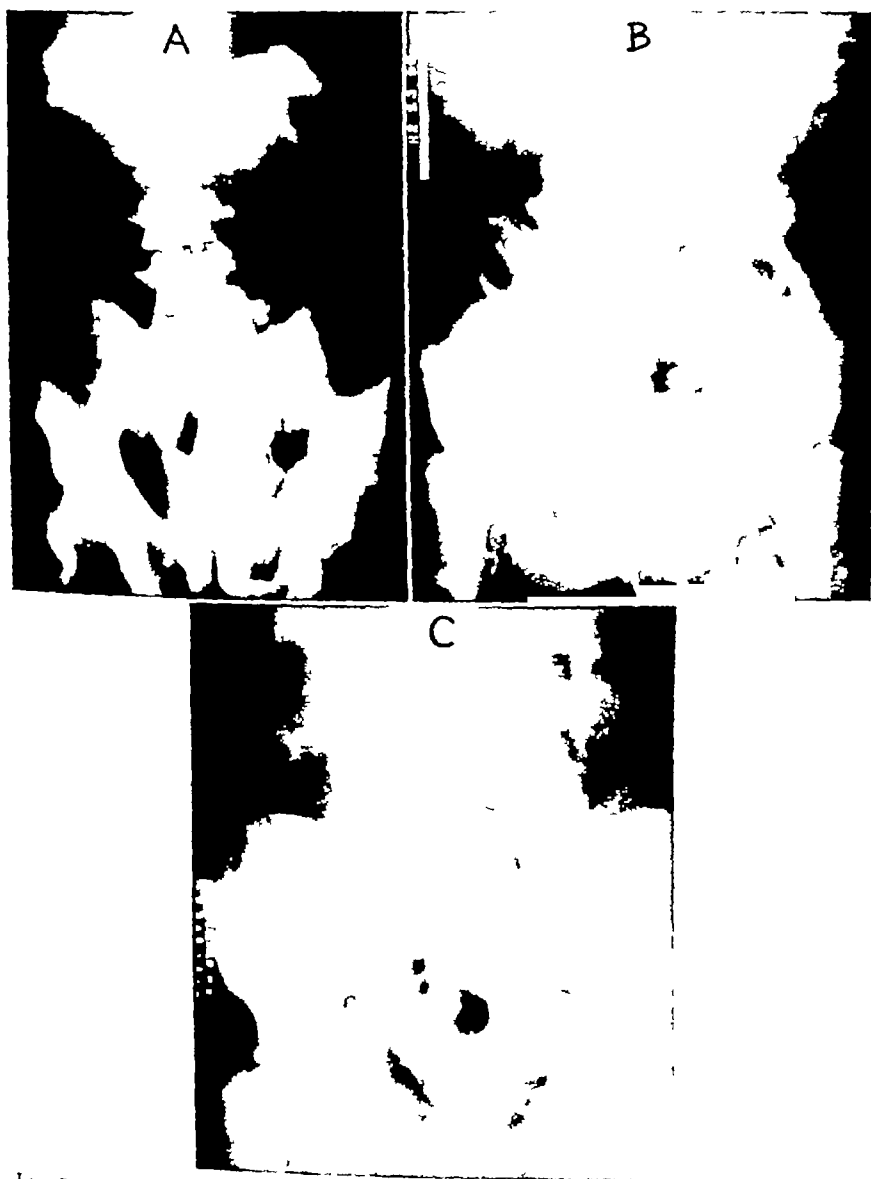


Fig. 1. A, Advanced carcinoma of prostate. Widespread lesions, predominantly osteolytic. B, Moderately advanced carcinoma of prostate. Osteoblastic lesions of right ilium and prostate. Rather rare pure osteolytic lesions involving pubic ramus, right iliac physis, 80 units. C, 20 per cent, and kidney 19 per cent. These are the commonest causes of the osteolytic lesions seen by the urologist. These metastatic lesions in conventional carcinoma of the prostate are usually *osteolytic* in appearance.

similar operation done, or, if deemed advisable, 10 days to 2 weeks may be allowed to elapse before operating upon the opposite side

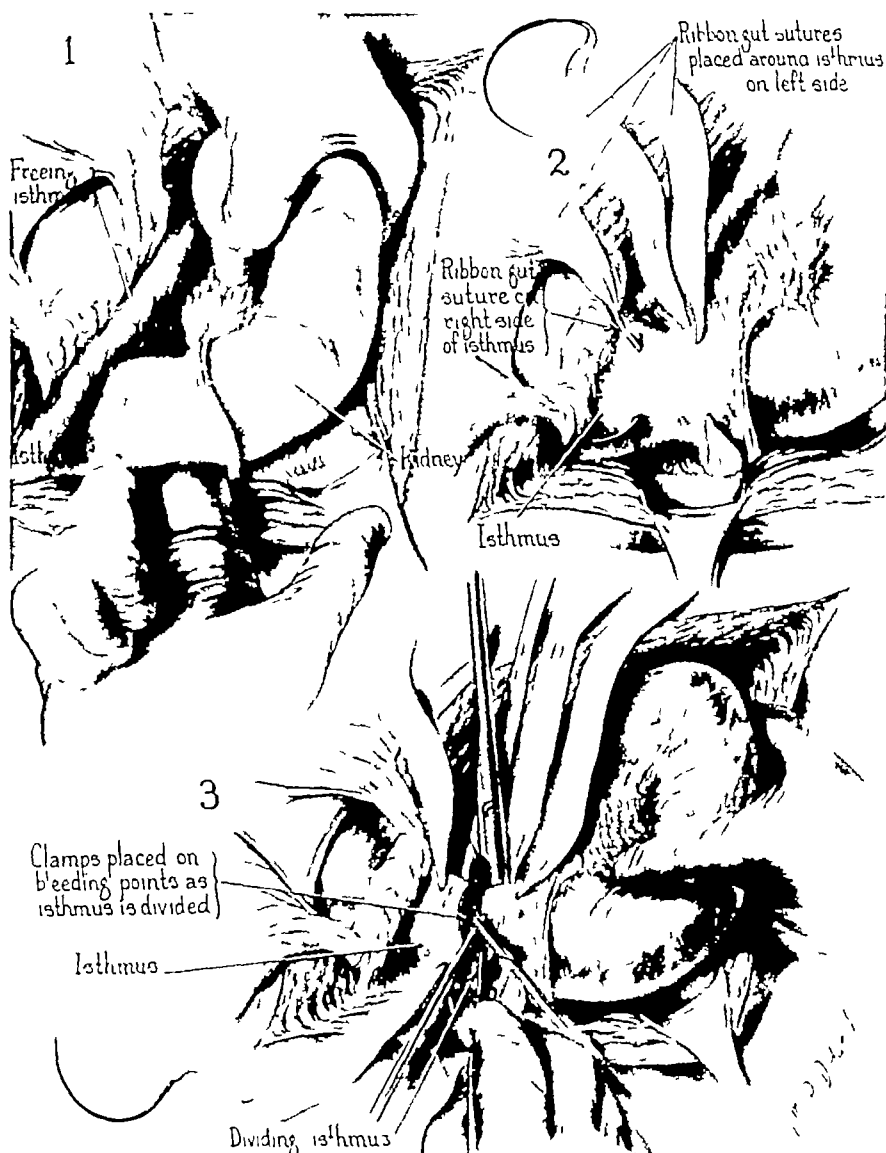


FIG. 3. 1, Freeing isthmus on posterior aspect by blunt dissection. 2, Placing ribbon gut sutures in isthmus preliminary to bisection. 3, Dividing isthmus, clamps placed on bleeding points.

Postoperatively, the splinting catheter and nephrostomy tube are left in place for 6 weeks.

In cases with abdominal pain due to the anomaly itself, but without hydro-nephrosis and infection, the isthmus is divided as described above and nephropexy performed on both sides.

LIPID CONSTITUENTS OF HUMAN MALE REPRODUCTIVE CELLS AS DETERMINED BY SUDAN BLACK B

ROYAL L BROWN

Studies on human spermatocytogenesis and spermiogenesis and on the mature spermium, using several staining techniques, have provided detailed knowledge of some aspects of the cytology of the human male reproductive cells^{1 2 3}. Recent cytochemical procedures for determining lipid distribution within cells, however, have not been applied previously to these stages nor to the mature spermium. This article, based on findings using human reproductive cells stained with sudan black B presents additional observations on the cytological and, by inference, the physiological nature of the procreative male elements, especially as pertains to their lipid constituents.

HISTORY AND PROBLEM EVALUATION

Ison,⁵ as early as 1936, recognized the comparative superior qualities of sudan black B as "very favorable for the demonstration of the smallest intracellular particles of lipid."

Subsequent cytochemical studies using this lipophilic stain have been reported on human blood and bone marrow cells,^{6 7 8 9} on bacteria,^{10 11} on yeast,¹² on intestinal protozoa,¹³ and on spermatozoa of man.¹⁴ The lipids in all instances were observed to be stained a blue-black color, this applies irrespective of

¹ Martin, J., Carnett, J. B., Levi, M. F. and Pennington, F. M. Study of morphology of human spermatozoa. University of Penn. Med. Bull., 1902, p. 2.

² Moench, G. L. Sperm morphology in relation to fertility. Am. J. Obst. and Gynec., 22: 199, 1931.

³ Gatenby, J. B. and Beams, H. W. The cytoplasmic inclusions in the spermatogenesis of man. Quart. J. Micro. Sci., 78: 1, 1936.

⁴ Williams, W. W., McGugan, A. and Carpenter, H. S. Staining and morphology of human sperm. J. Urol., 32: 201, 1934.

⁵ Ison, L. Sur de Nouveaux Colorants Histologiques Specifiques des Lipides. Compt. Rend. Soc. de Biol., Paris, 1936.

⁶ Phrington, J. J. and Wislocki, G. B. Histochemical methods applied to hematology. Blood, 3: 641, 1948.

⁷ Buhff, R. N. and Kimbrough, C. E. Studies on leucocyte granules after staining with Sudan black B and May-Grunwald-Giemsa. J. Lab. and Clin. Med., 32: 155, 1947.

⁸ Wislocki, G. B. and Dempsey, J. W. Observations on the chemical cytology of the normal blood and hemopoietic tissue. Anat. Rec., 96: 249, 1946.

⁹ Brown, M. I. and Wislocki, G. B. The localization of lipids in human blood and bone marrow cells. Blood, 5: 79, 1950.

¹⁰ Hartman, T. J. The use of Sudan black B as a bacterial fat stain. Stain Tech., 15: 190, 1940.

¹¹ Purdy, R. K. I., Stokes, I. C. and Kimbrough, C. E. Studies of the common aerobic fermenting bacilli. I. Staining for fat with Sudan black B safranin. J. Bact., 43: 717, 1952.

¹² Ehrlich, H., Haehn, H. and Hoerburger, W. The experiments on the synthesis of fats by microorganisms, with special reference to the work of the Institute for Fermentation. J. Biochem., 61: 680-723, 744, 1937.

¹³ Brown, P. I. Location of Lipids Within *Endamoeba coli* as Indicated By Sudan Black B. J. Urol., 65: 100, 1951.

¹⁴ Brown, P. I. Lipid Redistribution in human spermatogenesis as determined by Sudan Black B. J. Urol. & Cutan. Rev., 75: 531, 1951.

the right side (fig 1) Blood and urine cultures showed *Staphylococcus aureus*. The patient was operated upon as described above, the operation being done in two stages (figs 2 to 9) Postoperatively he was given sulfa therapy and the

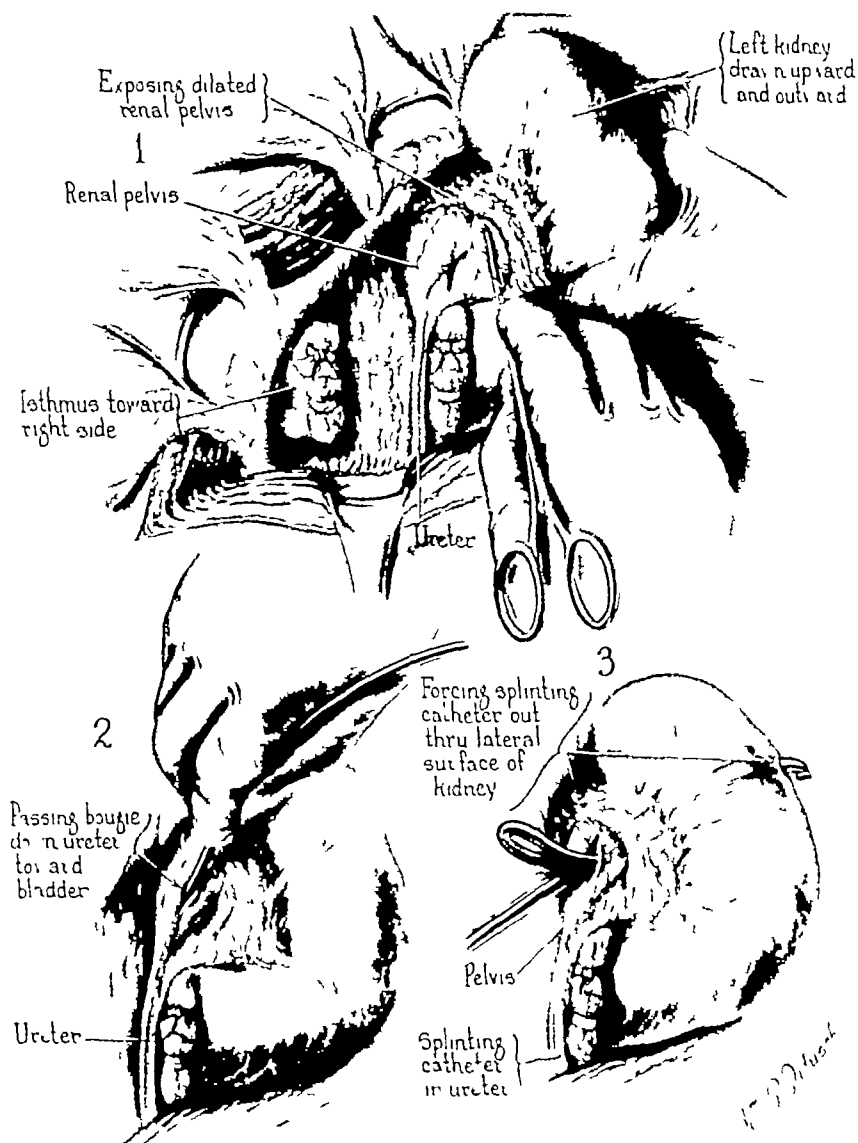


FIG 5 1 Left kidney drawn upward and outward exposing dilated pelvis. Ureter assumes a straight line with no constriction present, pelvis empties. 2 Passage of bougie down ureter through small incision made in pelvis to determine if obstruction is present. 3 Forcing splinting catheter out through lateral surface of kidney.

splinting catheters and nephrostomy tubes were left in place 6 weeks. Since then, he has had dilatation of the ureters at intervals and the condition of the kidneys has been followed by pyelography. He has been entirely relieved of his infection,

RESULTS

Organelles and other bodies which stain with sudan black B are quite numerous in all cells concerned in human spermatogenesis

Stained constituents of spermatogenic cells in

A Spermatocytogenesis During this phase of spermatogenesis the cells, following proliferation, undergo a meiotic division which results in haploid chromosomes. The initial cells of this process are the *primary spermatogonia*, they in turn give rise to the *secondary spermatogonia* and they to the *spermatocytes* which divide to form the *spermatids*

When stained with sudan black B the spermatogonium nuclear and cell membrane appear blue-black and slightly thicker than with chromatin dyes, iron hematoxylin, etc. The particulate condensations of the nucleus e.g., microsome etc. stain darkly and conspicuously. The *Golgi apparatus* (g) (fig 1 1 2), *centrioles* (c) and *mitochondria* (mit) of the cytoplasm also stain blue-black.

The secondary generations stain similar to the primary spermatogonia when using this sudan stain. The difference in their comparative cell size e.g. primary spermatogonia 10–12 μ and secondary spermatogonia 12–14 μ and the invariable absence of the crystalloid body within the cytoplasm distinguishes the larger secondary cells from the primary ones.

These secondary spermatogonia metamorphose, following division, into the *primary spermatocytes*. This division ends the so-called *period of proliferation* and the resulting spermatocytes commence their *period of growth*.

The *primary spermatocytes* during growth vary somewhat in size and nuclear structure; however, when fully developed they are large (15–25 μ) oval or spherical cells with a nucleus which approximates half to two thirds the diameter of the entire cell. The cytoplasm of the *secondary spermatocytes* is smaller (12–15 μ) and the nuclear content less conspicuous.

With sudan black B as with chromatin stains the first meiotic division is observable as it advances through the leptotene, the pachytene and the diplotene stages into diads and tetrads and finally the division of the cytoplasm into the two daughter secondary spermatocytes. The dynamic nuclear elements e.g. chromosomes etc. of spermatocytes are because of their lipid content evident especially during division stages. Similarly the metamorphic processes of meiosis and mitosis are delineated well with sudan black B by virtue of the lipid content of their centrioles, Golgi apparatus and derivatives (chromosome division phases) membranes and other concerned lipid-containing bodies. Other intracellular metamorphic changes essential to spermatogenesis consequently do become evident.

B Spermiogenesis The haploid *spermatids* (10–12 μ fig 1 1) arise during the maturation phase from the division of the secondary spermatocytes and through a series of transformations without cell division develop directly into the mature spermatozoa (*spermatozoan*) via spermiogenesis. Transformation is clearly apparent in the *acrosome* (a) which appears within the region occupied by the mitochondrion (mit) apparatus (g) and centrioles (c). From sections stained with

as there was some return of the pain, although her condition was greatly improved. The recurrence was not enough to persuade her to undergo a nephropexy on the opposite side, which probably would have relieved her entirely.

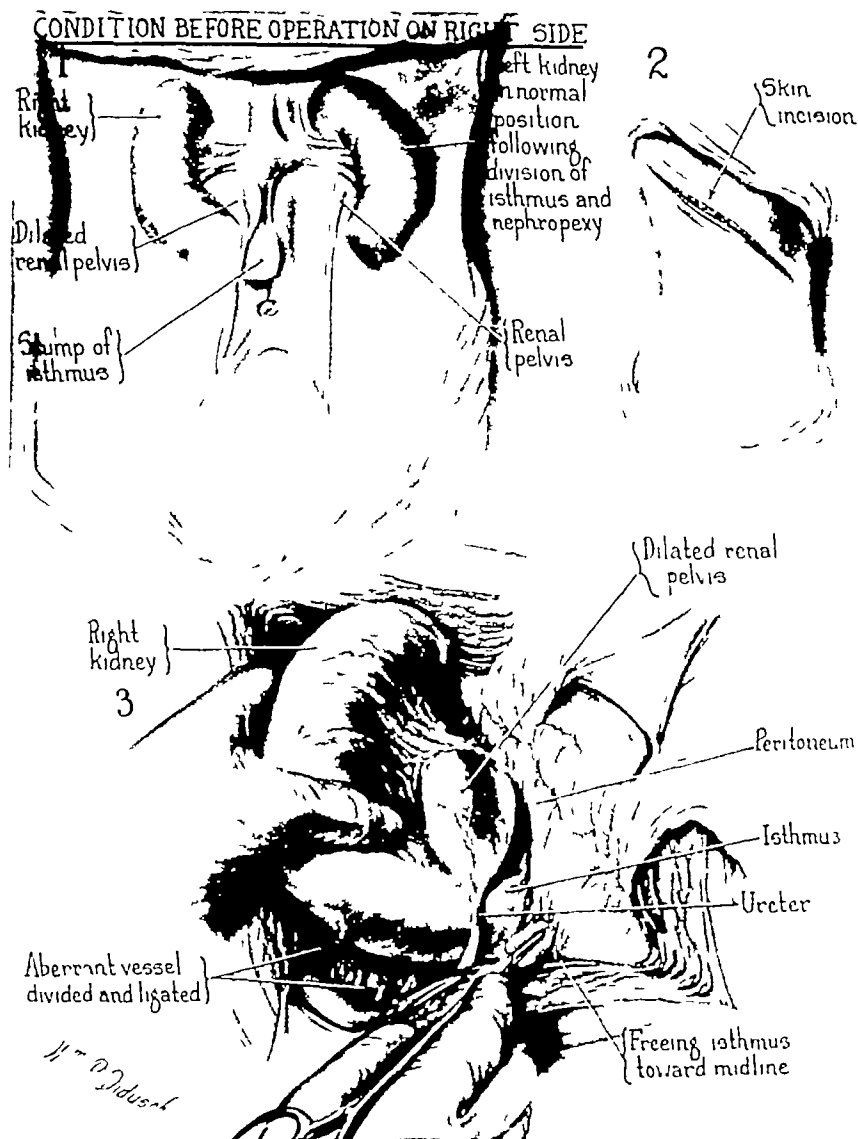


FIG 7 1, Condition present as result of first operation (division of isthmus and left nephropexy) 2 Incision to expose right kidney 3, Right kidney exposed, freeing isthmus toward midline

Case 3 Heminephrectomy for total destruction of the kidney on one side R. W., aged 40, was admitted to the hospital on October 28, 1932. Three days before, he had lifted a refrigerator and the following day had pain in the left side, which gradually increased. There was no nausea or vomiting and no urinary symptoms.

membrane, and migrate toward the cell membrane. Figure 1, 1 represents such an early spermatid ($10\ \mu$) with the centrioles (c) markedly peripheralward. The distal centriole (c^d) comes to lie adjacent to the cell membrane of the spermatid (fig. 1, 1), and the proximal one (c^p) which lies adjacent to it is usually interposed between it and the nucleus. This distal centriole gives rise to the primordium of the axial fiber (af, fig. 1, 2). The proximal centriole also appears to aid to a lesser degree in the fiber formation. This metamorphosing fiber continues to lengthen, widen and straighten out (fig. 1, 2, 3, 4, af) until it has attained its mature size ($50\ \mu$). A sheath, presumably secreted or acquired from the cytoplasm discard (fig. 1, 3) forms around this axial fiber throughout its length except for the terminal few microns. Together they form the mature flagellum (*tail*) of the spermium. Even at a moderately early stage of development, this axial fiber stains irregularly but heavily with sudan black B (fig. 1, 2-3). The *flagellar sheath* fails to stain, however, small globules of black staining materials which are interposed between the axial fiber and the sheath are fairly numerous (fig. 1, 4-19).

The *acroblast* (fig. 1, 1, ab) which is attached to the *anterior pole* (ap) of the nucleus and later (fig. 1, 2) opposite the centrioles (c) and axial fiber (af) contains the acrosome (ac). It is a lipid and chromatin staining body which occupies the center of the *clear area* (ca) of the *acroblast*. Figure 1, 2 shows an advanced stage of the usually hemispherical, blue-black acroblast (ab), containing the acrosome. This acrosome ultimately becomes the anterior half (fig. 1, 3), or more ($2\frac{1}{2}$ - $3\ \mu$) of the mature *head* region (3 - $10\ \mu$, usually about $5\ \mu$). It may contain other conspicuous lipid staining bodies (fig. 1, 3-19).

Several moderately large, lipid containing bodies are also present in the nucleus of the *spermatid*. The position of the nucleus within the cytoplasm (fig. 1, 2) assumes an eccentric position indicating that cell polarity attained through the approximation of the nucleus and the anterior cell wall is occurring as an initial step in the production of the *spermium head* (sph, fig. 1, 3). The chromatin meshwork (lum, etc.) of the spermiogenic spermatid nucleus stains surprisingly well with sudan black B, indicating the generous presence of lipids. The finely granular cytoplasm meshwork or reticulum, including its condensations (microsome) appears to contain even more lipids on the basis of the intensity of its staining reactions. The inter-reticular spaces remain unstained. The cell wall and plasma membrane together stain heavily blue-black and are conspicuously thick (fig. 1, 2, 3).

The two *centrioles* in fig. 1, 2 (c^d , c^p) have migrated from the cell membrane (cf. fig. 1, 1), to the nuclear membrane maintaining their close anteroposterior relationship to each other. Their position in relation to the acrosome indicate the intracellular *anteroposterior poles* (ap, pp, fig. 1, 2) of the metamorphosing spermatid. Thus is early delimited the symmetry of the spermium. The structural interval between the two centrioles which becomes the *neck* of the mature spermium remains nearly transparent with sudan black B. The cell is with other stains (fig. 1, 3). The *anterior knob* and *posterior end knob* are probable derivatives of the anterior and posterior centrioles. The *anterior knob* is blue-black with sudan black B. The *posterior end knob* is

probably representing massive destruction of the left kidney. Urine and pus drained through the abdominal wound, and a secondary anemia developed, along with toxic symptoms, and a septic temperature. The author first saw the patient

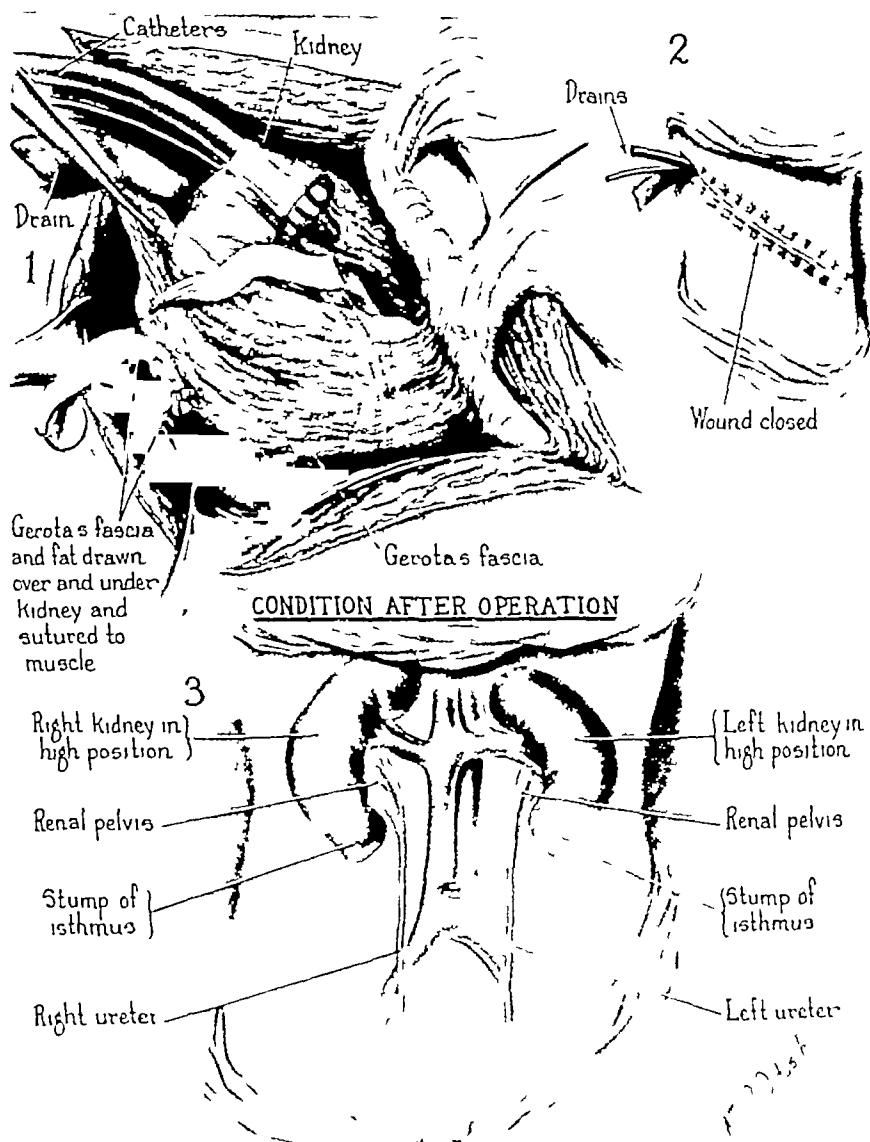


FIG. 9. 1 Gerota's fascia and fat drawn over and under lower pole of kidney and sutured to muscle to hold kidney in proper position for good drainage. 2 Wound closed, showing position of drains. 3 Condition present after second operation. Isthmus divided, both kidneys in high position.

20 days after the exploratory operation. A left nephrectomy was advised. His condition was such that it was necessary to transfuse him twice before operation. At operation an enormous sac was found replacing the left half of a horse-shoe

portion is stained blue-black and thereby helps to delineate the fragment. Other than these three spermia appear normal in morphology. Cytologically, they contain the blue-black stained structures previously mentioned.

Figure 1 7 and 8 are characterized by an oval *middle piece*. Its thick periphery is well as the cell wall of the nuclear portion of the head stain black. Its apparent increased thickness may be real as a normal or abnormal metamorphic characteristic or due to an overlapping fragment of the cell wall which has adhered closely. There are also several comparatively large blue-black globose bodies in the head and middle piece areas. A rarified area, the vesicle, is present in figure 1 7 also 5, 6, 10, 16, 17, and 18.

Figure 1 9 and 10 are megalocephalic forms with 10 shown in a lateral position. Figure 9 has retained the structural appearance of the unaffected nucleus of the spermatid with considerable mitochondrial-like elements scattered primarily peripherally. This may be a synctium of two heads or a single head with a symmetrical but abnormal portion of cytoplasm adherent to it. The middle piece and tail appear essentially within normal limits. The head and middle piece of figure 1 10 appear cytologically normal in spite of their increased size, the normalcy of the contained chromosomes may be the ultimate determining factor in its ability to fertilize an ovum.

Figure 1 11, 12, and 13 are normal mature spermia as observed from their lateral position. Figure 1 14 through 19 are side views of morphologically normal spermia. The variation in number, size, shape and position of sudan staining bodies in them is apparent, with emphasis upon variability. All figures are camera lucida drawings with exacting consideration for cytological details.

DISCUSSION

Lipids have been surmised to be essential constituents to vital processes and kinetic cytological elements for the past two or three decades. Recently, because it is conjectured that these lipids function in loose combinations with proteins and lipoproteins or other conjugates in vital functions of the cell, their relation to cytological structures has also become very important. Prior to this period the nucleus of a spermium or another cell had long been described as containing beside water and salts essentially nucleoproteins²² more recently deoxyribonucleic acid. Recent evidence indicates the presence of other significant constituents in the nucleus. Nuclei in general are now considered to contain structural functional lipids²³ as well as nucleoproteins²⁴ especially phospholipids and cholesterol. Kinetically important organelles of the spermium cytoplasm (e.g., chromatin, microblast, microsome, centrioles, Golgi, mitochondria, and their

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SURGERY OF THE HORSESHOE KIDNEY

OSWALD S. LOWSLEY

From The Oswald Srinney Lowsley Foundation, Inc. of St. Clare's Hospital, New York, N. Y.

The purpose of this paper is to call attention to the prevalence of horseshoe kidneys, to emphasize that such kidneys are more subject to secondary pathological changes than has been generally thought, and to suggest the type of treatment for various secondary lesions.

Because of its susceptibility to disease, as well as its relatively frequent occurrence, the fused kidney presents an important clinical problem. Almost every type of renal lesion has been encountered in horseshoe kidneys. With increased experience with this anomaly, the author has been impressed by the fact that a majority of the horseshoe kidneys seen clinically have hydronephrosis on one or both sides, with some degree of infection. Operation is often indicated, as in many cases cure cannot be obtained by the usual dilatation of the ureters and chemotherapy because of the anomaly itself. Once a horseshoe kidney becomes diseased, there is little hope of permanent relief except by surgical intervention.

Soon in 1888, was the first successfully to perform heminephrectomy in a horseshoe kidney, removing the hydronephrotic half. Heminephrectomy remains the most common operation, but all types of procedures have been performed, including pyelotomy, nephrostomy, pyeloplasties, ureterolysis, division of the isthmus, nephropexy, and repair of trauma.

INCIDENCE

The incidence of horseshoe kidney is uncertain. The incidence at autopsy varies from the 1/405 of Campbell, to the 1/1,000 of Davidson, the majority of writers placing it between 1/600 and 1/800. In his series of 47,483 autopsies, Campbell observed the anomaly twice as often in children (1/270) as in adults (1/542). Based on urographic examination, Dees found 4 cases in pyelograms on 1,410 consecutive patients (1/352). In our series, there were 46 cases in pyelograms on 13,089 patients (1/284). Judd, Brunsch and Scholl found the incidence among 2,124 kidney operations to be 1/112.6.

It is the general consensus that this anomaly is found at least two and a half times as often in males as in females.

DESCRIPTION OF THE ANOMALY—DIAGNOSIS

In horseshoe kidney, the renal organs are situated on either side of the spinal column, their lower poles usually being united by an isthmus which crosses the midline at the level of the fourth lumbar vertebra or lower. In fewer than 5 per cent of cases the upper poles are united, so that the concavity is downward. Not only are the kidneys displaced downward, they also lie closer to the spine than do separate organs. The pelves usually face anteriorly or medially, or they face laterally and away from each other with the ureters far apart. The

malleability than a 2 per cent solution. In our earlier experience with the clinical use of the material of bovine origin the original package as received from the manufacturer, containing 202 mg of dried fibrinogen, was slowly dissolved in 10 cc of physiological saline. Employing the operative technique described by Dees, this was mixed with 1000 units of thrombin dissolved in 2 cc saline by injecting the latter into the lumen of the catheter employing a hypodermic needle. Thus the fibrinogen and thrombin solutions were admixed immediately before they entered the renal pelvis and the process of coagulation in the presence of this high thrombin concentration began almost instantly. In referring to table 2 it will be noted that the onset of clotting is definitely delayed by diluting the thrombin solution and that the resulting coagulum is definitely tougher and of greater tensile strength. In fact, it has been found that if 1000 units of

TABLE 1 *Property of coagulum (with thrombin 1:25/cc)*

FIBRINOGEN SOLUTION	HUMAN		BOVINE		
	Dees	Cutter			U50/cc
Per cent of protein	2	9	2	9	9
Onset of clotting (seconds)	30	39	37-43	30	28
Tensile strength (grams, 8 mm cylinder)	24-90	110	67-72	165	150
Tensile strength (grams, 8 mm @ 37°C)	82-100	—	72-80	—	—
Dissolution time (hours, urine)	18-24	12	8	12	11

TABLE 2 *Studies of coagulation time (with fibrinogen solution, 2%)*

THROMBIN SOLUTION		TIME OF ONSET (SECONDS)		FIRM CLOT (SECONDS)	
U/cc	%	Human (Dees)	Bovine	Human (Dees)	Bovine
125.0	10.00	—	11	—	36
62.5	5.00	10	11	30	25
31.3	2.50	15	26	45	55
25.0	2.00	30	37	60	62
15.6	1.25	45	—	180	—

thrombin were dissolved in 40 cc of saline and only 1 cc of this solution were mixed with the 10 cc of fibrinogen solution, 9 per cent, either of human or bovine origin, a coagulum of such tough consistency resulted that the dissolution of any portion of it which might remain in the renal pelvis might conceivably be so slow that it could become a source of trouble or obstruction. Further investigation, however, indicated that if 1000 units of thrombin were dissolved in 20 cc physiological saline, 1 cc of this solution when mixed with 10 cc fibrinogen solution (9 per cent) formed a coagulum which appeared to reach a more than adequate tensile strength after 5 to 10 minutes. Further experiments indicated that any remnant which might inadvertently be left within the renal pelvis or calices should dissolve completely in urine within 11 hours.

The material of bovine origin was tested on two kidneys obtained at a necropsy. In one of these four calculi averaging less than 1 cm in diameter were placed in the pelvis along with over a thousand particles of sand. The pelvis

of renal mobility and pressure or drag upon the vessels 4) interference with free renal circulation, which may lead to some degree of nephritis.

As a rule the symptoms of secondary pathological changes are the same as when these ailments occur in nonfused kidneys, and the conditions should be treated the same as similar lesions in nonfused organs, with heminephrectomy done for disease of major import (tumor, tuberculosis, extensive destruction, etc.) When conservative surgery is undertaken for stone or gross infection the obstructive factor causing stasis should be corrected at the same time, if practicable.

Correction of the secondary pathological changes has not always resulted in complete subsidence of the symptoms. Many surgeons now believe that when conservative surgery is done for secondary lesions, preserving both halves, division of the isthmus with suspension of the separated kidneys by nephropexy should be performed in order to obviate the danger of persistence of symptoms attributable to fusion alone.

Occasionally the secondary renal lesion does not produce symptoms and is discovered accidentally during examination for some other reason. Then even though there are no symptoms, the condition may require surgery (as in tumor).

Occasionally also, secondary renal changes may produce symptoms which are not referable to the kidney itself. For example, Chesterman, in 1941, reported a case of acute intestinal obstruction due to massive hydronephrosis of the right side of a horse-shoe kidney resulting from obstruction by an accessory artery.

The hydronephrotic right half of the kidney was removed, with cure of the symptoms.

Group 3 Horseshoe kidneys with no secondary pathological change, but with definite symptoms referable to the anomaly itself. These cases, which apparently are not numerous, were thoroughly discussed by F. E. B. Foley in 1940 in an excellent paper. The predominant symptom is pain in the umbilical area with or without gastro-intestinal disturbances, due to pressure upon the great vessels and adjoining nerves by the isthmus or the ectopic renal masses.

The diagnosis is made by not finding any extrarenal lesion causing the symptoms and no renal disease other than the anomaly. Such patients have frequently been operated upon for the relief of symptoms ascribed to the appendix, gall-bladder, etc. without relief of their symptoms and in many cases horse-shoe kidney has been diagnosed accidentally during abdominal surgery (nonrenal).

Therefore it would seem advisable that patients with unexplained epigastric pain especially if accompanied by gastro-intestinal disturbances, have the benefit of an excretory urogram before exploratory operation is undertaken.

Surgeon treatment in these cases consists in division of the isthmus (symptom only) with suspension of the separated kidneys by nephropexy.

CAUTION: OVERLAP FOR HYDRONEPHROSIS AND INFECTION IN HORSESHOE KIDNEY

Hydronephrosis and infection of one half of a horse-shoe kidney may have as their chief indication to require heminephrectomy. In many cases, however, conservative surgery is indicated particularly when the condition is bilateral.

ing stay sutures or Allis forceps. The snug fit renders a pursestring unnecessary. The ureter is then lightly occluded for which we have found a small rubber-protected arterial clamp satisfactory. The renal pelvis is then gently filled with physiological saline and is repeatedly flushed, the capacity is noted. Great care has been taken not to exceed the amount of the estimated capacity when employing fibrinogen-thrombin mixture of bovine origin. The appearance of free bleeding would be considered a contra-indication to the use of such a mixture for obvious reasons. It is highly desirable that its use be entirely of a topical character and none be permitted to gain access to the circulation because of the possible harmful effect of a foreign protein. In the cases in which it has been

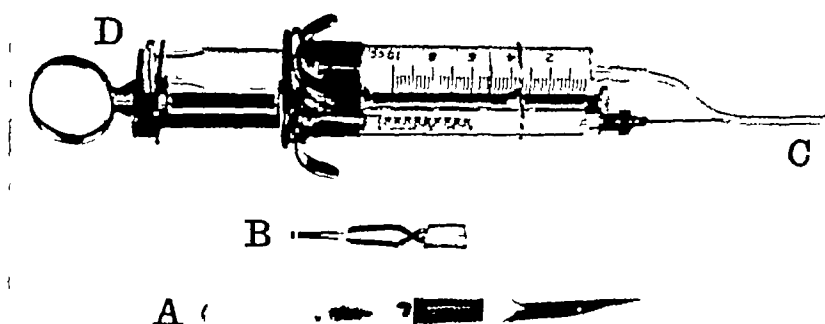


FIG. 2 Special instruments facilitating coagulum pelvolithotomy. Small puncture in renal pelvis is made with spear pointed scalpel (A) after lightly clamping ureter with rubber protected "bull dog" type of clamp (B). Short length 12 to 14F catheter cut on sharp bias (C) is inserted through puncture and solutions of fibrinogen and thrombin contained in 10 cc, and 1 cc syringes respectively are injected simultaneously, facilitated by holding device (D). *

used in this way no harmful effects have been observed. The injection of the solution of fibrinogen and thrombin respectively should be made simultaneously. This has been facilitated by placing both syringes in a holder designed for the purpose (fig. 2), which permits the injection synchronously of both solutions although there is only 1 cc of the thrombin solution as compared with 10 cc fibrinogen. Figures 3 and 4 serve to illustrate the roentgenograms of some of the clinical cases in which this technique has been employed together with the coagulum recovered revealing the contained stones.

We have not used a solution of aerosol OT, as advised by Dees, in the preliminary lavage of the renal pelvis nor has the fibrinogen solution been preheated to 37°C as he has suggested. These are mentioned as possible additional advantages which we have not used in our limited experience. The increased tensile strength obtained by a higher fibrinogen concentration appears to render preheating of the fibrinogen solution unnecessary.

* We are indebted to Mr. Fred J. Wallace, Pres. American Cystoscope Makers, Inc. for his invaluable assistance in designing the synchronizing syringe holder.

The kidney is then fixed in position by a nephropexy which is performed either by the ribbon-gut method, or by utilizing Gerota's fascia as a shelf to hold it in

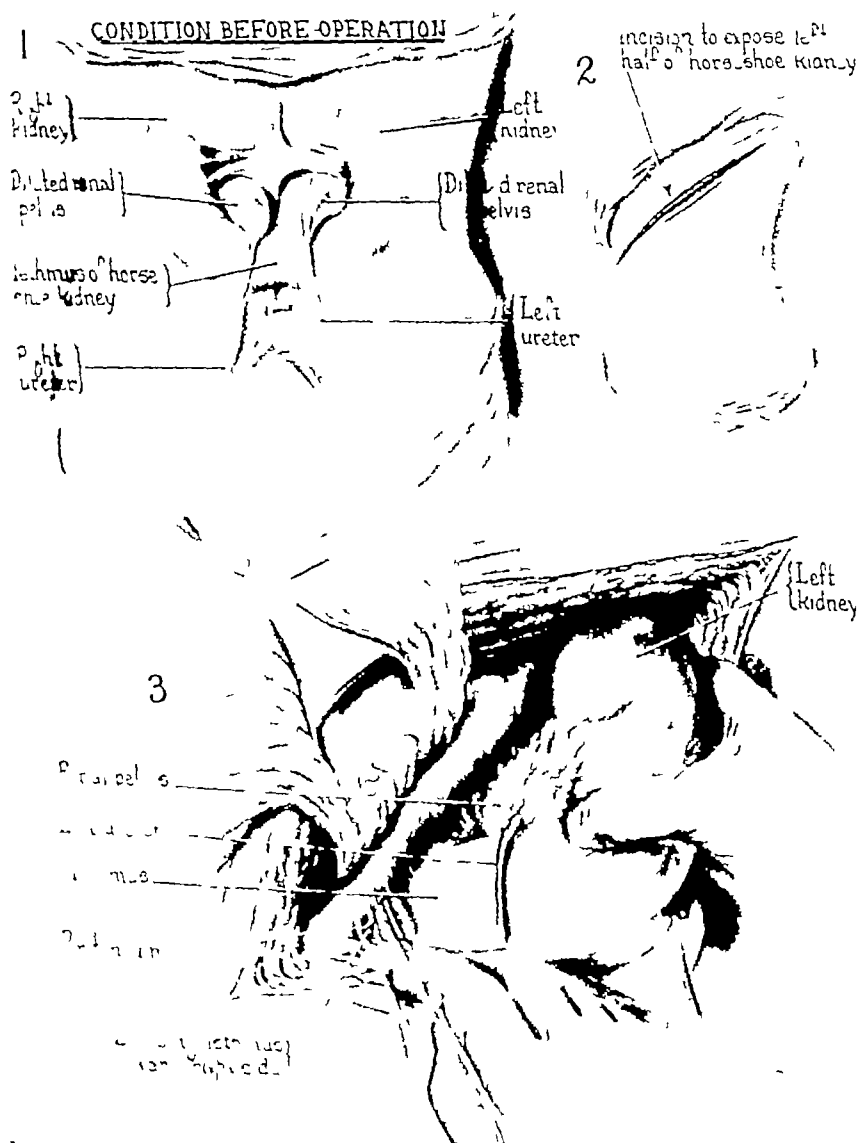


FIG. 2. Operation: division of isthmus, bilateral splinting of ureter and nephrostomy tube; 1. Nephropexy. 1. Condition present before operation, shows relation of dilated pelvis to horseshoe kidney. 2. Incision to expose left half of horseshoe kidney. 3. Exposing

portion. A drain is inserted and the wound is closed in layers, the two catheters of the drain being brought out at its upper angle.

If the patient's condition warrants, he may be turned on the other side and a

the pyelotomy. In some cases when the pyelotomy is enlarged, the extrusion appears spontaneously with the almost dramatic effect of bringing with it multiple large and small stones which can be clearly seen included in the coagulum. Obviously, in a case where a calculus is incarcerated in a calyx with an infundibulum too narrow to accommodate the stone, the use of this technique would be unsuccessful. Although Dees originally had advised only partial closure of the pyelotomy to permit the expulsion of any clots remaining, this precaution has not been observed by us and no harm has resulted in our experience by closing the pyelotomy tightly, reinforced with a pad of fat. Closure of this type has been preferred in all pyelotomies in an effort to protect the incision from the associated urinary infection so common in these cases.

SUMMARY

Fibrinogen and thrombin derived both from human and bovine sources have been compared in various dilutions experimentally as to their characteristics with special reference to the optimum percentage of protein, the onset of clotting time, the tensile strength of the coagulum and the dissolution time of the clot in urine. The bovine material compares favorably with that of human origin and in some respects may be regarded as superior.

There is evidence that the optimum dilutions of the material in physiological saline may be regarded as 9 per cent fibrinogen and thrombin containing 50 units per cubic centimeter. A mixture of these solutions in the proportion of 10 cc fibrinogen to 1 cc thrombin produces a coagulum within 5 minutes of a tensile strength measuring 155 grams employing a cylinder of coagulum 8 mm in diameter and of a consistency more than adequate for coagulum pelvolithotomy. It has been found that a clot of this degree of firmness will dissolve in the urine within 11 hours.

The experimental and clinical use of such a preparation in a limited number of cases of nephrolithiasis indicates that it may be used safely in coagulum pelvolithotomy in the human.

Modifications and improvements in the usual technique are offered for the procedure including a smaller aperture in the renal pelvis, rendering unnecessary the use of a pursestring. A device is presented which facilitates the simultaneous injection of the solutions of fibrinogen and thrombin.

The availability of fibrinogen and thrombin of bovine origin should contribute definitely to the more widespread employment of coagulum pelvolithotomy. The authors discuss some of the advantages, disadvantages, contraindications and precautions derived from their experience with this technique in a limited number of cases.

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CITATION OF ILLUSTRATIVE CASES

(Case 1 Conservative surgery (division of isthmus, bilateral splinting of ureter and nephrostomy, bilateral nephropexy) for hydronephrosis and infection W F, an

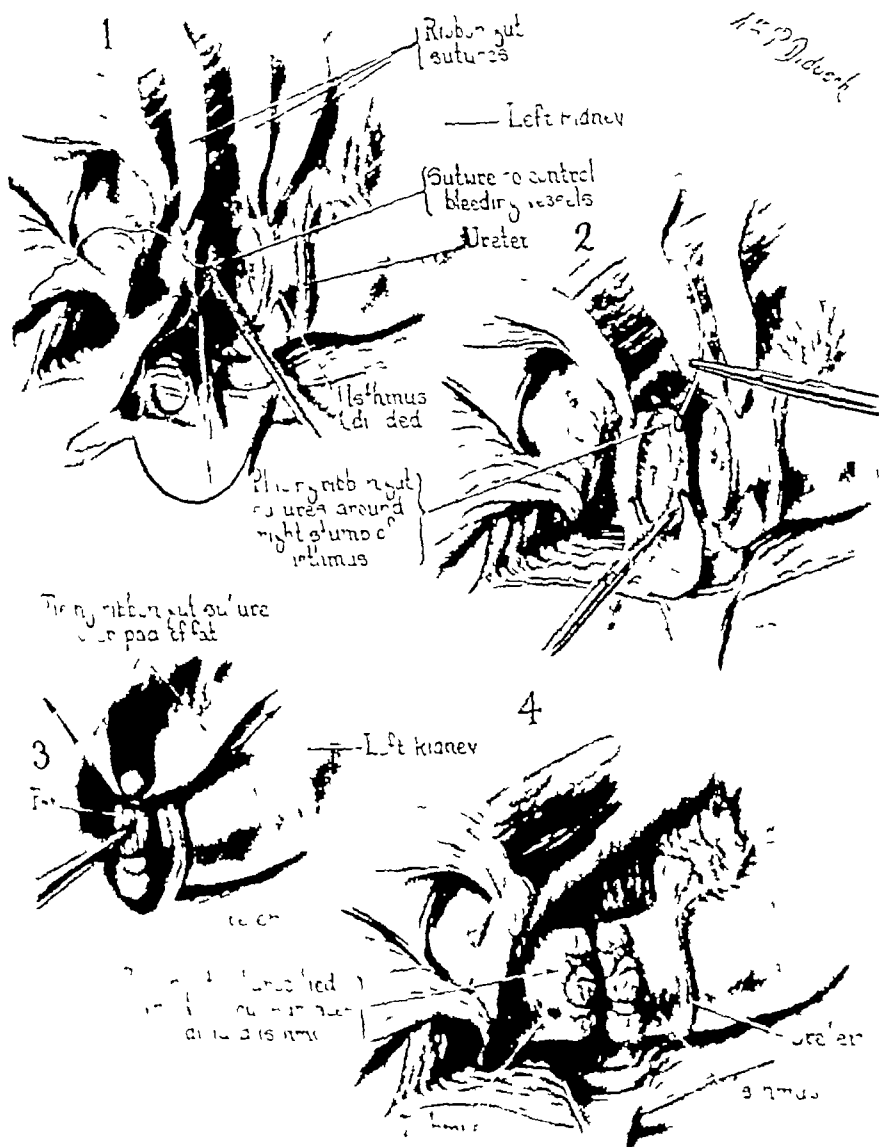


Fig. 3 1 Isthmus divided placing suture to control bleeding vessel 2 Placing ribbon gut sutures around stump of isthmus on right side 3 Tying ribbon gut suture over pad of fat on cut surface of isthmus 4 Ribbon gut sutures tied over fat on cut surface of divided

11 Case of H. F. was referred to the author in October 1944 because of emphysema. Intravenous and retrograde pyelograms disclosed a horseshoe kidney with bilateral hydronephrosis and infection at the ureteropelvic junction and hydronephrosis more marked on

postoperative aeration of the lung. If the phrenic nerve is not crushed or blocked, the motion of the diaphragm in most cases does not interfere with the operation. The diaphragm is incised in line with the incision. Care is taken to avoid cutting into any organ adherent to the underside of the diaphragm, into the liver on the right side or the colon or spleen on the left side.

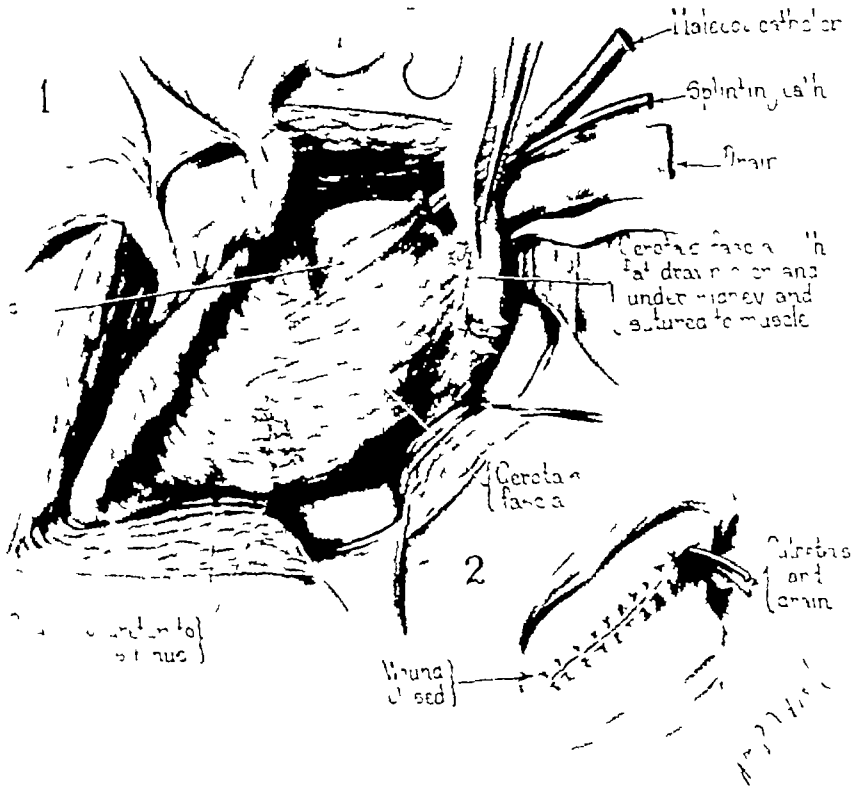
A Finochietto rib retractor is used to separate the ribs. The renal mass then actually bulges into the wound. The spleen or liver can usually be retracted easily out of the field. If the spleen interferes with the operation, it can be removed. The renal tumor is gently retracted laterally, the duodenum on the right, or the colon on the left side, is carefully freed, and with very little handling, retraction or dissection, the renal vein and artery are easily exposed, clamped, sectioned, and ligated individually. The ureter is isolated, cut, and ligated. The renal mass is then removed with all adherent fat, capsule or peritoneum. Any enlarged nodes in the region of the pedicle, aorta or vena cava are easily palpated and can be removed. The peritoneum is closed to reperitonealize the raw area. If deemed advisable, the renal bed may be drained through a stab wound in the loin. The diaphragm is closed with interrupted sutures of heavy silk. The pleural cavity is drained through an interspace above the incision with a Pezzer catheter from which the head has been cut leaving only a flange. The injection of long lasting, local anesthesia in oil into the intercostal nerve of the rib resected and into the intercostal nerve above and below the incision, tends to prevent postoperative pain and encourages deep breathing. After the lung has been re-expanded the chest incision is closed with interrupted sutures of silk or continuous sutures of No. 1 chromic catgut. The cut edges of the costal margin are accurately apposed and sutured with silk or fine steel wire. The peritoneum is closed with a continuous suture of catgut, and the abdominal muscles in layers with a continuous suture of chromic catgut or interrupted sutures of silk, and the skin with a continuous suture of silk. The catheter is aspirated and clamped off to be connected to an underwater trap when the patient is returned to bed. The catheter is removed on the second or fourth postoperative day. Drainage of the pleural cavity is not considered a necessity by all thoracic surgeons, some preferring repeated aspiration of the pleural cavity to remove fluid and air. Nasal oxygen is employed for 24 hours and the patient is encouraged to sit up on the first or second postoperative day or as soon thereafter as possible.

There were no deaths or serious complications in our 6 cases that are being reported. They stood the operation well, the blood loss and shock were less than usually occur with the removal of large renal tumors or densely adherent kidneys by the lumbar or transperitoneal route. There were four females and two males, the youngest being 36 years of age and the oldest 58. Their average age was 49 years.

They remained in the hospital 11, 12, 14, 17, 23 and 26 days following the operation. Case 2, Miss V. O'B., remained in the hospital 17 days after the operation. She was able to leave the hospital on the twelfth postoperative day but wished to remain until she was able to travel alone. In case 6, Mrs. R. J.,

and there is now no hydronephrosis on the left side and only slight hydronephrosis on the right side

Case 2 Division of isthmus and nephropexy (left side) for abdominal pain due to horseshoe kidney J. A., a 64-year-old female, was referred to the author for treatment of a horseshoe kidney with hydronephrosis, which had been diagnosed elsewhere by excretory and retrograde pyelograms. For 14 years she had had attacks of pain in the right upper quadrant and epigastrium which had increased



1. 6. 1 Nephrostomy tube (Malecot catheter) splinting catheter and drain in place
2. 6. 2 Wound closed. Catheters and drain emerging

frequency and for 7 years had been almost continuous. There was also constipation and abdominal distention. One year earlier she had had a cholecystectomy at which time a retroperitoneal mass was found. Postoperatively the pain became worse. A gastro-intestinal series was negative. Excretory and retrograde pyelogram showed a horseshoe kidney with bilateral hydronephrosis, more marked on the left side. Operation—division of the isthmus and a left nephropexy was done on November 9, 1947 and the patient was discharged 9 days later. Postoperatively she had dilatation of the ureters at intervals of several months.

and artery clamped, divided and ligated individually. The ureter was divided and ligated and the kidney was then dissected free and removed (fig 2). The pleural cavity was drained with a Pezzer catheter inserted between the eighth

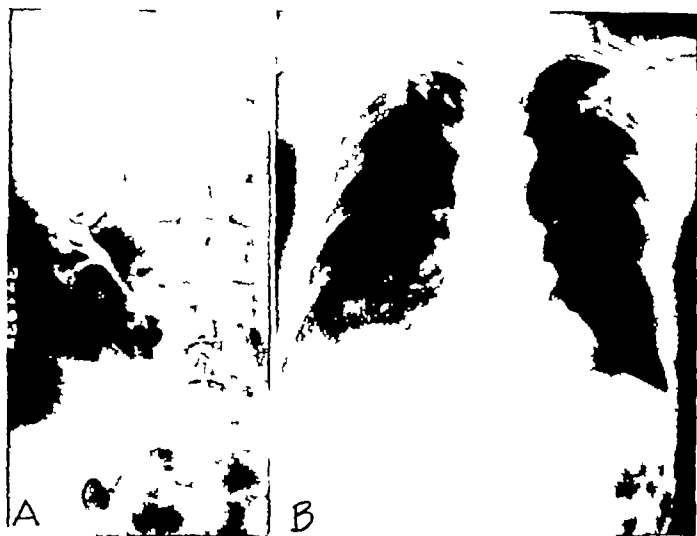


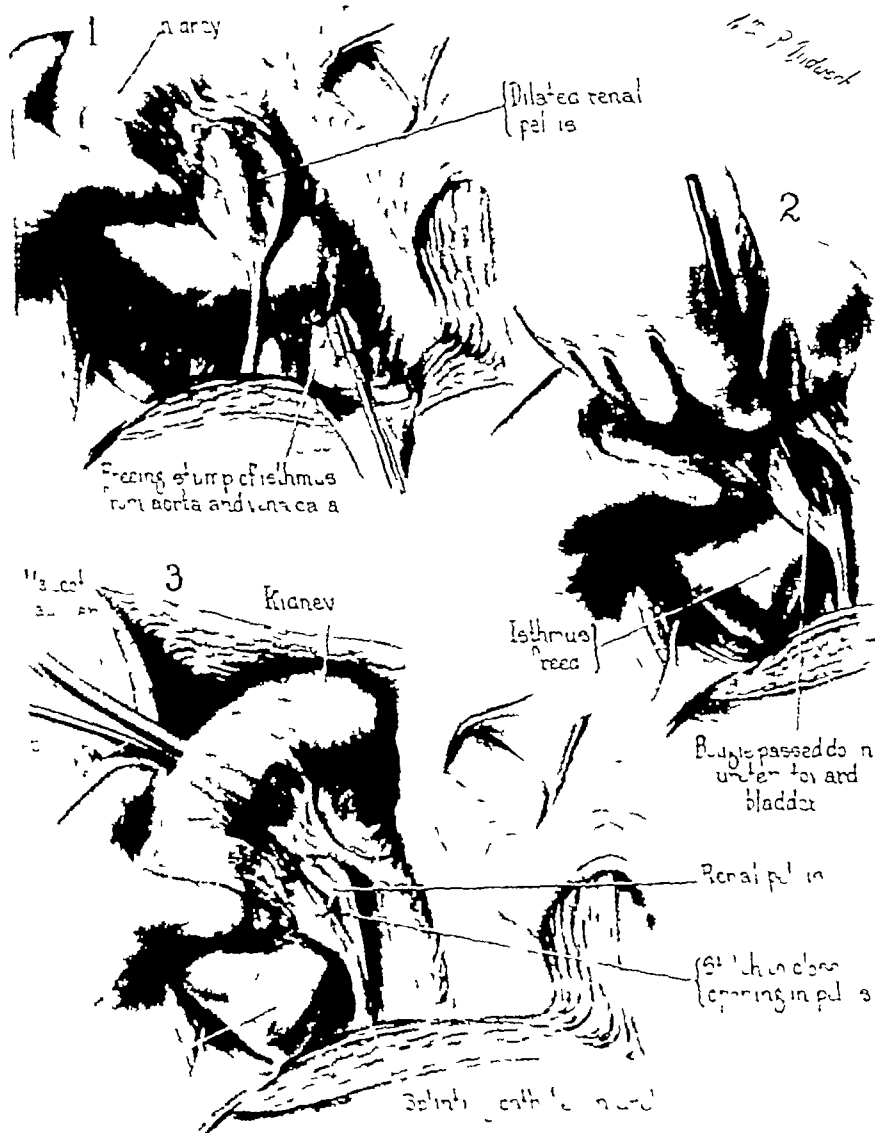
FIG 1 Case 1 A, tumor, upper pole of right kidney. Arrows marked upper limit of tumor. B, x-ray of chest, third postoperative day.



FIG 2 Case 1 Kidney bisected. Adenocarcinoma, upper pole and ninth ribs. The condition of the patient was excellent throughout the entire procedure. He received 1000 cc blood during the operation.

Immediate postoperative course was uncomplicated. The lung had completely re-expanded in 48 hours and the Pezzer catheter was removed (fig 1, B). On the

Physical examination revealed a large hard, circumscribed and tender mass in the left side of the abdomen. Exploratory operation through a left rectus incision showed this mass to be retroperitoneal. Two hundred cubic centimeters of brown-



1. Freeing stump of isthmus from aorta and vena cava by blunt dissection. 2. Isthmus freed. Bougie passed down ureter through small incision in pelvis. 3. Suture catheter in ureter and Malecot catheter in pelvis of kidney for drainage. Suture catheter in the pelvis.

4. Mass aspirated and the mass drained through the abdomen. Fourteen days later examination showed what was thought to be a normal sized right kidney. 5. A circumscribed mass on the left side having the shape of a kidney.

in the midaxillary line in the eighth interspace with a Pezzer catheter. The patient tolerated the procedure extremely well. She received 500 cc of blood during the operation.

The entire postoperative course was very satisfactory, the highest temperature being 100F. The lung had completely re-expanded in 48 hours, and the Pezzer catheter was removed (fig 4, C). The patient was discharged on August 15, 1949, with the wound well healed.



FIG 4 Case 2. *A*, left unilateral, polycystic kidney. *B*, kidney bisected. Polycystic kidney. *C*, x ray of chest, fifth postoperative day.



FIG 5 Case 3. *A*, right kidney pelvis outlined to show deformity. *B*, kidney bisected. Renal carcinoma. *C*, x ray of chest, seventh postoperative day. Note fluid level. Five hundred cubic centimeters of fluid and air aspirated.

Microscopic diagnosis was "polycystic kidney disease with chronic pyelonephritis."

Case 3. W. T., a 58-year-old white man, was admitted to the hospital October 17, 1949, with a history of pain in right flank, gross hematuria, nausea and vomiting of 2 days' duration. He gave no history of previous hematuria. For 2 years he had had moderate progressive symptoms of prostatism, some weight loss during the past few months, and severe arthritis for 25 years.

Physical examination revealed slightly enlarged heart, right flank and lower quadrant tenderness but no mass, and marked kyphosis and ankylosis of spine.

The retrograde pyelogram revealed a normal left kidney. The right kidney pelvis showed distortion and dilatation with a pressure defect involving the pelvis and lower calyces (fig 5, *A*). Throughout the right renal area there was

kidney this extended far down into the pelvis. Heminephrectomy was done, removing the sac. The pathological report showed calculous pyonephrosis with complete loss of renal structure. Postoperatively the wound drained profusely but when the patient was discharged, 6 weeks after the heminephrectomy, was well healed except for a very small sinus.

Comment. This is a case of pre-existing hydronephrosis and calculus of the left half of a horseshoe kidney, which was activated by trauma and treated by transperitoneal drainage (all advised) and finally by heminephrectomy, with good results. The patient died 13 months after removal of the destroyed kidney due to a carbuncle on his arm with profound toxicity which evidently affected his remaining kidney.

SUMMARY AND CONCLUSIONS

In our series, there have been 46 cases of horseshoe kidney in pyelograms on 13,080 patients (1/284).

Horseshoe kidneys are much more subject to disease than are nonfused organs due mainly to the abnormal insertion and course of the ureters, the regularly anomalous vascularization, and fixation of the fused kidney by its isthmus to the surrounding structures and vessels.

Horseshoe kidneys may exist without evidence of disease and without producing symptoms.

A common condition affecting horseshoe kidneys is hydronephrosis with infection and, quite frequently, calculus. Much rarer are tuberculosis, polycystic disease, solitary cysts, pyonephrosis, nephritis, tumor, and trauma.

Horseshoe kidneys, by their position, may cause pressure on the great vessels and other viscera, resulting in abdominal pain with or without gastro-intestinal disturbances. Removal of the appendix, gallbladder, or other organ has not infrequently been done without relief of the pain until the kidney has been bisected and placed in its proper position by nephropexy.

Extensive destruction of the kidney and tumor require heminephrectomy.

Conservative surgery is indicated in many cases of hydronephrosis and infection especially when bilateral. The operation utilized by the author consists of 1) division of the isthmus, 2) dilatation of the ureter with a splinting catheter,

3) nephrotomy or ureteropyeloplasty as indicated, and 4) nephropexy. The catheter and nephrostomy tube are left in for 6 weeks.

Division of the isthmus either for the purpose of removal of one-half of the kidney or for relocating the separated organs is easily accomplished by perfect hemostasis by using the fat-and-ribbon-gut method of repair of the isthmus described above.

I wish to express my grateful appreciation to Mr. William P. Diduch for the excellent series of drawings which add so greatly to this presentation.

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Cystoscopy revealed chronic cystitis with toothpaste-like pus exuding from the left ureteral orifice. A 6F catheter was passed to each kidney pelvis and 40 cc thick pus with a marked colon bacillus odor aspirated from the left kidney. The urine from the right kidney was clear. There was normal excretion of indigo carmine from the right kidney and none from the left. The retrograde pyelogram



FIG 6 Case 3 Healed wound

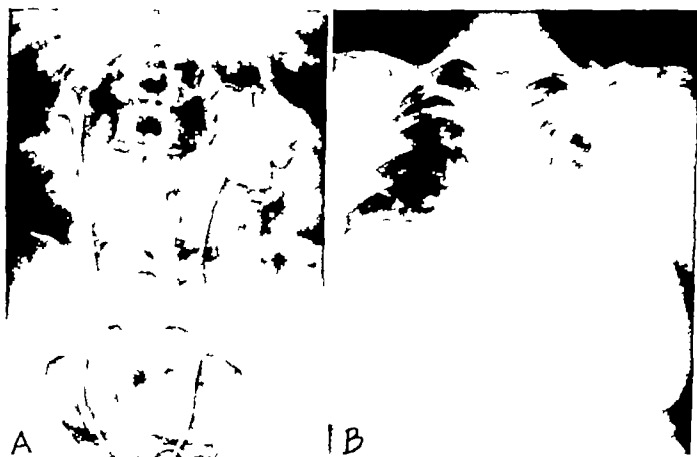


FIG 7 Case 4 A, left pyonephrosis B, x ray of chest fourth postoperative day revealed a normal right kidney and a large left pyonephrosis (fig 7, 1). There were no shadows to indicate stones.

The urologist who did the ureterolithotomy reported that due to marked adhesions around the kidney, the patient's short stature and obesity, he did not believe that the kidney could be removed by a lumbar incision. With this advance information it was decided that the thoraco-abdominal approach would be the safest and easiest for the patient. A catheter was left indwelling to the left kidney for 3 days during which time sulfadiazine, penicillin, and streptomycin were given.

COAGULUM PELVIOLITHOTOMY, AN IMPROVED TECHNIQUE

THOMAS D. MOORE AND THEODORE H. SWEETSER, JR.

*From the Department of Urology, John Gaston Hospital, College of Medicine,
University of Tennessee, and the Moore Clinic, Baptist Memorial Hospital,
Memphis, Tenn.*

In 1943 Dees described the use of a coagulum composed of a mixture of human fibrinogen and thrombin ingeniously designed to facilitate the removal of small stones from the renal pelvis and calyces after performing a pyelotomy. He and his co-workers conducted a carefully controlled laboratory investigation with observation of the mechanism involved in coagulum formation and had made accurate notes on the optimum dilutions along with the time of the onset of the coagulation process and period required for its maximum development. Although advantages of the procedure were at once apparent, its widespread adoption has been hampered by difficulty in obtaining the material together with its rather exorbitant expense. Several reports, however, have appeared in the literature including those of Harrison and Trichel, and Hoffman who also comment on the advantages they have noted in its use. Hoffman reported a case in which many small calculi were recovered which had not been revealed by the roentgen examination; this is a distinct advantage of the technic.

Although human fibrinogen and thrombin were available for a limited time from at least one commercial source, in 1949 its production was discontinued apparently because the small demand for the product had rendered its manufacture an unprofitable venture. Prior to this we had used coagulum pelviolithotomy in a few cases with much satisfaction. When the material was no longer available our disappointment led us to search for other sources. When one considers that its use for this purpose is essentially a topical application it did not seem unreasonable to employ fibrinogen and thrombin other than of human origin. Inquiry among several possible sources revealed that fibrinogen of bovine origin could be had from at least one manufacturer of biologicals and a supply for experimental and clinical use was obtained.*

EXPERIMENTAL DATA

In the earlier reports Dees outlined and tested several factors he regarded as necessary for an ideal coagulum employing material of human origin. In our experiments we have been able to compare these properties with coagulum of bovine origin as revealed in table 1. The percentage of thrombin in the clot apparently affects both the rapidity of the clotting and the tensile strength. If a small amount of thrombin is present greater catalytic activity takes place and the long molecules merge into shorter fibers more rapidly, productive of a jelly-like clot of poor tensile strength. A comparison of this effect is noted in table 2. It has also been found that a solution of fibrinogen of either type with a concentration of 9 percent yielded a clot of greater strength and greater

* Manufactured by Department of Chemical Investigation, Parke Davis & Company, Detroit, Mich., to whom we are indebted for some valuable suggestions.
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Presented at the Southern Section, American Urological Association Meeting, Memphis, Tenn., May 1951.

There was a large, firm, slightly tender mass in the left upper abdomen extending into the flank. The blood pressure was 200/120. An upper gastro-intestinal tract series was negative but did show an extrinsic mass in the left upper quadrant. The excretory urogram was unsatisfactory.

February 1, 1950, several hours after a barium enema, there was severe cramping in the upper abdomen. Examination revealed marked anemia, the blood pressure was 90/60. The patient was admitted to hospital and given one unit of plasma and 2000 cc blood during the next 36 hours. She responded rapidly and the blood pressure stabilized.

The preoperative chest film was negative for metastases.

All laboratory findings were within normal limits except for a lowered red count and hemoglobin.



FIG. 9. Case 5. A, left kidney displaced and rotated. B, x-ray of chest, fifth postoperative day.

The retrograde pyelogram revealed a normal right kidney, the left kidney was pushed downward and medially, and rotated laterally. The left upper calyx was elongated (fig. 9-A). The function of each kidney was good and the urine negative for pus. The most likely diagnosis was a renal cyst but a retroperitoneal tumor was considered.

On February 17, 1950, a left thoraco-abdominal nephrectomy was done, employing pentothal and intratracheal cyclopropane, nitrous oxide, ether and oxygen anesthesia. The line of incision was over the tenth rib, extending downward medially across the abdomen to the lateral border of the rectus muscle. The tenth rib was resected subperiosteally close to the spine. When the pleural cavity was entered, the lung was found to be adherent to the parietal pleura by a number of fine adhesions; these were divided. The diaphragm was incised in line with the thoraco-abdominal incision. A large cystic, retroperitoneal mass was found adherent to the adjacent structures and attached to the left kidney. In freeing this mass, the splenic capsule was torn. There was moderate hemorrhage, and a splenectomy was done. The renal vein, artery and the ureter were isolated, clamped,

was then filled with the fibrinogen-thrombin mixture and upon removal of the resulting coagulum all of the stones and sand were recovered and the pelvis and calices appeared clear of the foreign material. In the pelvis of the other kidney were placed four stones and seven smaller stony particles which were clearly visualized in a roentgenogram. After injection of the fibrinogen-thrombin mixture and a delay of approximately five minutes, the fairly firm coagulum recovered all of the stones (fig. 1)

CLINICAL USE

So far coagulum pelviolithotomy using material of bovine origin has been used in 7 cases, 3 men and 4 women varying in age from 23 to 60 years. In 6, nephrolithiasis was unilateral and there were multiple stones, some of which



FIG. 1. Roentgenogram of kidney removed at necropsy in which were artificially placed four larger and seven smaller calculi, all of which were immediately recovered. Note the clearing of the pelvis and calices with the contained calculi. Fibrinogen-thrombin mixture of bovine origin used.

were quite small or sand-like, the removal of which ordinarily would have been attended with some difficulty. In one of these a calculus measuring about 1.5 cm. in diameter appeared to have been displaced ahead of the coagulum as it formed. Many smaller sandy particles, however, were included in the coagulum. After extrusion of the clot, the larger calculus was removed separately with forceps. The concentration of the solution which we are now using with its longer coagulation time should prevent this occurrence. In the earlier cases the technique as described by Dees and more recently by Harrison and Frichel was used in which a 4 mm. pyelotomy was made through which was introduced a 12 to 14 F. catheter. We have learned through experience that a purse-string is desirable even if a mere puncture is made in the posterior aspect of the renal pelvis with a spear-pointed knife. Leakage at this point has been mentioned as a complication in 10 to 15 per cent of reported cases. A short segment of rubber catheter prepared by dividing it in such a way that there is a sharply pointed end can easily be introduced into the puncture with the aid of support-

dicumerol. Anticoagulant therapy was continued for 14 days during which period the course was very stormy, marked by fever, abdominal distention, and nausea and vomiting. After anticoagulant therapy had been discontinued and the prothrombin activity had risen to 64 per cent, a bilateral superficial femoral vein ligation was done. The convalescence was essentially uneventful and after the

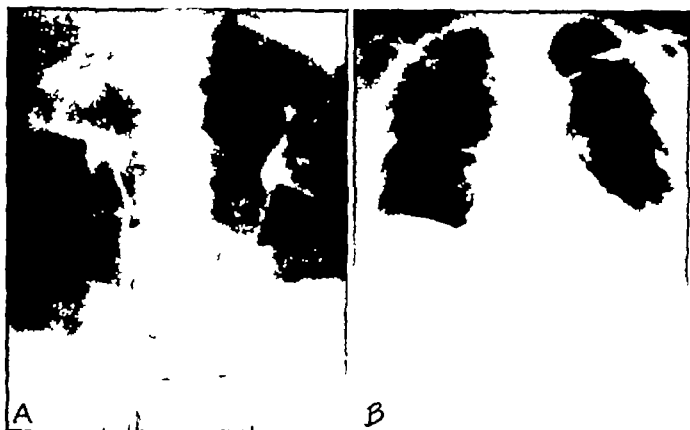


FIG 11 Case 6 A, tumor, upper pole of right kidney B, x ray of chest, sixth postoperative day



FIG 12 Case 6 Healed wound. Developed postoperative abscess of middle and lower end of incision

wound had healed, the patient was encouraged to get out of bed until she was completely ambulatory.

On September 19, 1950, a right thoraco-abdominal nephrectomy was performed, employing sodium pentothal and intratracheal nitrous oxide and oxygen anesthesia. The line of incision was over the eleventh rib and extended downward and medially to the lateral border of rectus muscle. The eleventh rib was resected subperiosteally near the spine. After entering the pleural cavity, the diaphragm was opened and the incision carried through the abdominal musculature to the lateral border of the rectus muscle. The renal vein, artery and ureter were each

In conclusion it might be mentioned that a small intrarenal pelvis precludes the use of this technique. One disadvantage that might be mentioned is that a larger pyelotomy is necessary than would ordinarily be made in order to permit



FIG. 3. A preliminary roentgenogram. Note 3 small shadows in right renal area. The upper and lower were identified by the excretory urogram (B) as intrarenal. C, the two calculi embedded in coagulum which formed a cast of the renal pelvis and calyces.



FIG. 4. A preliminary roentgenogram with multiple shadows (3) in left renal area. B, excretory urogram (B) as a calculous obstruction opposite fourth transverse with marked degree of pyelectasis in which there are two smaller calculi. C, excretory urogram (C) showing a cast of the renal pelvis and calyces containing 3 stones, the one at outlet having been displaced above obstruction at time of injection.

extrusion of the coagulum. No harm will result from this if the incision is made in the region of the ureteropelvic juncture toward the midportion of the pelvis with the renal parenchyma rather than transversely. The incision should be lightly compressed with the idea of extruding the coagulum rather than the employment of traction for its withdrawal through

A NEW SIMPLIFIED METHOD FOR TRANSRENAL PYELOSTOMY

ALFONSO DE LA PEÑA AND LUIS PALOMEQUE

From the University of Madrid, Spain

Sometime ago we developed a method of inserting a nephrostomy tube with the aid of a malleable stylet. The method, although an improvement on previous methods, presented some difficulties. The tip might be detached from the stylet while endeavoring to locate the calyx through which the tube had to be placed. If the malleability was excessive, the force to be applied did not drive the nephrostomy tube into the exact position chosen, but with dexterity all these minute points were easily overcome.

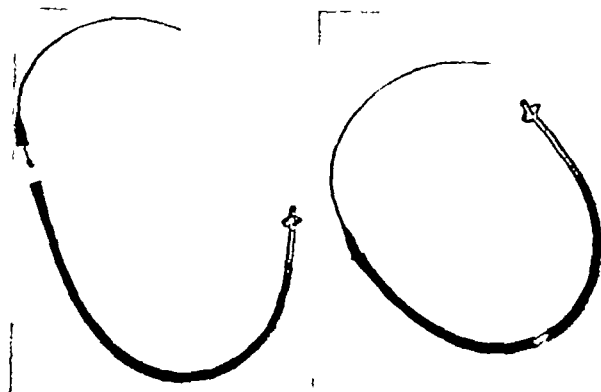


FIG 1

Nevertheless, one of us (A. P.) suggested a modification of the method that seemed to be the easiest technique so far developed.

The illustration (fig. 1) is self-explanatory. A catheter (Cummings, Foley, Pezzer, Malecot) is fitted inside the barrel and the distal end of the stylet fitted. The union of the whole system is so snug that the more traction one exerts, the closer is the adjustment.

Through a pyelotomy incision the point of the stylet is inserted and the calyx into which the drain is to be inserted is catheterized. Light pressure will make the point of the stylet appear at the convex border of the kidney. Traction will drive the proximal end of the catheter in sight, and reversal of the steps to adjust the system will release the catheter. Adjustment of the catheter so that it will remain in the best draining position is easily accomplished.

THORACO-ABDOMINAL NEPHRECTOMY

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From the Department of Urology, Medical College of Alabama, Birmingham, Ala

In presenting the thoraco-abdominal approach for difficult nephrectomies, we do not wish to leave the impression that it is the ideal incision, and without fault. The main objections to the incision are 1) Two separate cavities are opened, 2) it requires intratracheal anesthesia, 3) chest complications pneumonia collapse of lung and empyema, while rare, may occur, they may also occur with any of the other incisions, 4) while not an absolute necessity a thoracic surgeon is a welcome member of the team.

Through the usually employed incisions large renal tumors cysts the fixed or frozen kidney and patients with kyphosis or scoliosis of the spine offer prospect of the most difficulty and at times impossible nephrectomy. The ideal incision for large renal tumors must meet the following requirements 1) Excellent exposure, 2) early ligation of the renal vein and artery and other large vessels to prevent hemorrhage and squeezing tumor cells into the vascular system 3) reduction of trauma to prevent shock, 4) the removal of the kidney with as much of the perinephric fat and capsule of Gerota as possible, 5) adequate exposure for the removal of enlarged lymph nodes in the region of the renal pedicle porta and venous and metastatic areas in adjacent organs. The thoraco-abdominal incision meets all these requirements. Any incision that fails to do so does not offer the lowest morbidity and mortality.

For the operation the patient is placed in the usual kidney position. At times in kyphosis of the spine it may be necessary to use the kidney elevator. In the majority of cases the exposure is excellent without its use. A stomach tube is employed to insure an empty stomach. Intratracheal anesthesia is used and the lungs kept almost completely expanded during the operation. Due to the excellent exposure less muscular retraction and relaxation are required, and the depth of anesthesia and amount of anesthetic agent used are reduced. The skin incision follows the rib or interspace that gives the best exposure and extends across the abdomen to the lateral border of the rectus muscle near the level of the umbilicus.

If a rib is to be removed it is resected subperiosteally as close to the spine as possible. This prevents the ligaments from binding the ribs together and gives the best exposure. The pleural cavity is entered through the selected interspace into the pleural bed. If there are adhesions between the parietal and visceral pleura they are separated by sharp dissection. The chest incision is continued down the abdomen to the lateral border of the rectus muscle. The phrenic nerve is crushed to stop the motion of the diaphragm. If it seems desirable the muscular action of the diaphragm return soon to help with respiration. The phrenic nerve may be injected with 2 per cent novocain thus permitting the diaphragm to return in one or two hours and insures better



FIG 1 Cystogram with sodium iodide. Ureteral backflow shows gigantic hydro uretero nephrosis of remaining kidney 22 years after left nephrectomy for tuberculosis. Examination 9 years previously had shown a similar condition.

(cystogram with ureteral backflow) carried out in 1940 and 1949 showed an identical picture. Furthermore, during these 9 years the patient's general condition has been excellent except for occasional attacks of urinary infection and high blood urea which disappeared after streptomycin therapy.

Alcala 98, Madrid, Spain

the postoperative stay was 23 days. She remained in the hospital to take deep x-ray therapy that was started on the twelfth postoperative day. In case 1, Mr. J. J. I., the postoperative hospital days were 26. He was able to leave the hospital on the sixteenth postoperative day but remained to have a transurethral resection of the prostate done.

The operation was performed 3 times on each side.

The tenth rib was removed 4 times and the eighth and eleventh rib 1 time each. The eighth rib was removed in case 3, since the patient had a renal cell carcinoma of the right kidney, complicated by marked kyphosis and ankylosis of the spine.

The microscopic diagnoses were adenocarcinoma, polycystic kidney (unilateral), renal cell carcinoma, pyonephrosis ("frozen kidney"), renal cyst with hemorrhage, and clear cell carcinoma.

The highest postoperative temperatures were Case 1, 102°F on the eighth postoperative day due to urinary retention and infection and in no way related to the operation. Cases 2, 3, 4, and 5 were 100.4°F or less. Case 6 was 101°F the first postoperative day.

The thoracotomy tube was removed in 48 hours in 2 cases, and in 72 hours in the 4 remaining cases. There were no chest complications, case 3 required a thoracentesis on the seventh postoperative day to remove 500 cc air.

All patients received penicillin or penicillin and streptomycin during the first few postoperative days.

The number of malignant cases reported are too few and the length of time elapsed since the operation too short, to make any statement regarding the end results. We believe that this operative technique should improve the end results and chances of cure in renal tumors.

CASE REPORTS

Case 1, J. J. I., a 54-year-old white man, partial paraplegic, was admitted to hospital June 23, 1949, with history of gross hematuria of 5 days' duration and micturition bladder symptoms for several months. There had been a 25 pound weight loss in the past year. The prostate was enlarged grade 1 to 2 and there was no evidence of carcinoma. Two ounces of residual urine was obtained. A tumor could be palpated in the right renal area. Cystoscopy revealed contracture of the bladder neck and there was no evidence of a bladder tumor. The retrograde pyelogram revealed a large filling defect in the upper pole of the right kidney (Fig. 1). The preoperative chest x-ray was negative for metastases and the preoperative x-ray determinations were within normal limits. Preoperative diagnosis: Tumor of the right kidney.

On July 15, 1949, a right thoraco-abdominal nephrectomy was done using a combination of endotracheal and intratracheal nitrous oxide, oxygen and other anesthetics. An incision was made over the tenth rib and the rib was resected subperiosteally. The incision continued downward and medially across the abdomen to the lateral border of the rectus muscle. The diaphragm was incised in line with the incision. The renal nerve lightly crushed. The renal pedicle was exposed, the vein

In a series of 116 cases of duodenal fistula selected from the literature, plus 12 cases from the Massachusetts General Hospital, Bartlett and Lowell⁴ found that 22 were secondary to right nephrectomy. The overall mortality rate of this total series was 38 per cent. These authors were of the opinion that the most important single factor in local care is the use of constant suction to keep the wound dry and prevent contact between the duodenal contents and abdominal wall. As an additional safeguard, they advocated local applications:

1) Chemical neutralization of the proteolytic ferments by combining them with an excess of peptone powder, protein and fat, beef juice or Bovamine.

2) Mechanical adsorption of the ferments by finely divided charcoal, Kaolin, or bronzing powder.

3) Inactivation of the tryptic ferments by producing an acid medium accomplished by irrigating the wound with N/10 HCl or 5 per cent tannic acid.

4) Protection of the surrounding skin with boric acid, zinc oxide, or liquid latex.

5) Elimination of positive intra-abdominal pressure by passing a tube into the duodenum.

Warshaw⁵ and Potter⁶ likewise advocated local applications and wound irrigation on the premise that these are clinically effective and physiologically sound. Warshaw stated "prolonged application of a combination of Witte's peptone (10 per cent in saline) and N/10 HCl will cure duodenal and other intestinal fistulae in most cases."

LePoutre and Dupas,⁷ in reporting 15 cases discovered in the literature, mentioned the use, in conservative treatment, of tube drainage of the fistula, gradually decreasing the diameter of the tube until the tract closed spontaneously. The surgical method advocated by these authors, after rejection of primary closure and gastro-enterostomy, is jejunostomy, with gastro-enterostomy and exclusion of the pylorus as a later phase, if the condition of the patient will permit.

CASE REPORT

A white male, aged 40, was admitted ambulatory to Letterman Army Hospital with a history of recurrent episodes of right flank pain, varying from dull aching in nature to sharp, stabbing, intermittent attacks. These episodes were frequently initiated by exercise and associated with nausea and vomiting. The pain radiated inferiorly.

The past medical history was of significance in that the patient had eleven previous hospitalizations, eight of which were due to symptoms referable to the right kidney, starting with a perinephric abscess 16 years prior to present entry and treated by incision and drainage.

No positive findings were elicited on initial physical examination other than some tenderness in the right flank and an old, well-healed right lumbar scar.

X-ray examination of the chest, lumbar spine, and urinary tract (excretory

⁴ Bartlett, M. K. and Lowell, W. H. *New Eng. J. Med.*, **218**: 287, 1938.

⁵ Warshaw, D. *Am. J. Surg.*, **27**: 130, 1935.

⁶ Potter, C. J. *A. M. A.*, **88**: 890, 1927.

⁷ LePoutre, C. and Dupas, L. *Arch. d. mal. des org. gen. urin.*, **5-6**: 712, 1931.

eighth postoperative day the temperature was 102F. Catheterization revealed 3½ ounces of infected residual urine for which an indwelling catheter was placed. Penicillin and sulfadiazine therapy was instituted and the temperature was normal in 48 hours.

On August 5, 1949, a transurethral resection of bladder neck was done with no difficulty or complications. The patient was discharged on August 10, 1949 (fig. 3).

The microscopic report was adenocarcinoma, right kidney.

(Case 2) V. O'B., 36-year-old white woman was admitted to the hospital July 26, 1949 with a history of "pulling" sensation with slight soreness in left flank of 4 months duration. A mass was noted in left flank 6 weeks previously. She



FIG. 3. Case 1. Healed wound.

had had no weight loss, hematuria or urinary symptoms. The left upper quadrant of the abdomen was filled with a nodular, mildly tender, freely movable mass. Retrograde pyelograms revealed a normal right kidney. There was a deformity of the left pelvis and calyces consistent with a tumor or a unilateral polycystic kidney (fig. 4 A).

The chest x-ray was negative for metastases and the preoperative laboratory examinations were within normal limits.

On July 27, 1949, a left thoraco-abdominal nephrectomy was done employing a skin pentothal and intratracheal nitrous oxide-oxygen and ether anes-

thesia. The line of incision was over the tenth rib and extended downward and laterally across the abdomen to the lateral border of the rectus muscle. The tenth rib was removed subperiosteally. The diaphragm was opened in line with the incision and the phrenic nerve crushed. The left renal mass protruded into the thorax and was found to be a polycystic kidney. The right kidney was examined and no evidence of polycystic disease found. The renal vein and artery were ligated individually and the ureter sectioned and ligated. The mass was then removed (fig. 4 B). The pleural cavity was drained

The patient's general condition improved rapidly, although he continued to drain a large quantity of what appeared to be digested fat through his flank wound for three or four days. No bile drainage was evident. The abdominal wound healed promptly and the flank incision was healed in three weeks.

COMMENT

Duodenal injury in right renal surgery, though fortunately uncommon, is a very serious complication with a mortality of as high as 85 per cent in some reported series. It is our opinion that surgery is definitely the treatment of choice, however, to be effective, the condition must be recognized early and the fistula closed without delay. Primary suture of the defect following mobilization of the duodenum is sufficient, provided the defect is closed before digestion of tissues has progressed to the point where there is edema and friability of the margins of the hole to the extent that sutures would tear through. Delay in repair also results in changes in blood chemistry to a critical level, which alters the postoperative prognosis.

Conservative treatment, even if recovery ensues, results in prolonged convalescence, digestion of tissues, constant nursing, and vigorous therapy to counteract chloride depletion, sodium bicarbonate loss from bile and pancreatic juices, alkalosis secondary to loss of HCl, dehydration, azotemia, depletion of serum protein, and rapid manition.

Duodenal perforation incident to renal surgery should be handled as would be intestinal perforation from any other cause. Surgery for this complication is not the formidable procedure it once was, due to improvement in technique, anesthesia, a better understanding of blood chemistry and the availability of antibiotic agents.

SUMMARY

A case of duodenal fistula is presented which resulted from a stitch injury that was incurred in a right Deming nephropexy and which recovered following surgical repair of the duodenal perforation.

Surgical treatment is recommended for this complication. Early recognition, prompt repair, sound postoperative care directed toward maintenance of electrolyte and fluid balance, and the use of antibiotics to control infection should greatly alter the deplorable mortality statistics of the past.

a fairly large, homogeneous density. A preoperative chest film was made but was unsatisfactory. (Through error it was not repeated before surgery.)

Preoperative laboratory studies were within normal limits except for leukocytosis.

On November 4, 1949, a right thoraco-abdominal nephrectomy was performed using pentothal and intratracheal nitrous oxide and oxygen anesthesia. The incision extended along the course of the eighth rib and downward and medially across the abdomen to the lateral border of the rectus muscle. The eighth rib was resected subperiosteally near the spine. The base of the lung was adherent to the diaphragm by dense, fibrous adhesions. By sharp dissection, the lung was freed from the diaphragm and an incision made in the diaphragm in line with the abdominal incision. The right border of the liver was found to be adherent to the peritoneum by adhesions which were freed by sharp dissection. An incision was made in the peritoneum over the renal pedicle, and the renal vein and artery were dissected out and ligated. The ureter was freed, sectioned and ligated and the kidney was then removed with an area of peritoneum attached to it (fig 5, B). This prevented closure of the posterior peritoneum. The renal fossa was drained through a stab wound in the lumbar region, and the pleural cavity with a Pezzer catheter through the sixth midaxillary interspace. The blood pressure was stable and the patient's condition excellent during the entire procedure. He received 500 cc of blood on the table.

The immediate postoperative course was complicated by shock 30 minutes after the patient was returned to bed. He responded rapidly to 500 cc of blood and oxygen. On the second postoperative day a chest x-ray revealed marked fibrosis of right lung, probably the result of an old tuberculosis. There was no evidence of active disease or metastases. At this time the lung was completely expanded and the Pezzer catheter was removed.

The temperature reached 100F on the first three postoperative days, then remained normal until the sixth postoperative day when it reached 101F. At that time chest x-ray revealed a definite fluid level in the right chest just above the diaphragm with numerous areas of encapsulated air (fig 5, C). A thoracentesis was done and 500 cc of air but no fluid removed. The temperature was normal the following day and remained normal until the patient was discharged on the 13th postoperative day (fig 6).

The microscopic report was "renal carcinoma."

CASE REPORT. A 49-year-old white woman was admitted to the hospital on July 7, 1950 with history of passing two small calculi 7 years previously and a lumbar ureterolithotomy 2 years later. She had had persistent left flank pain for the past 5 years with gross hematuria, chills and fever at frequent inter-

vals. Physical examination was negative except for obesity and tenderness to palpation in the right flank.

Her urine and left kidney urine were loaded with pus and gram negative gram positive bacilli. The urine from the right kidney was negative for organisms. The hemoglobin was 70 per cent and the bladder contained about 40 per cent in 1 hour.

considered of pelvic origin and therefore must have been situated either in the abdomen or retroperitoneum and was filling the pelvis from above. Under constant observation for the next 4 days the patient's abdomen grew to the extent of a term pregnancy, but still no definite diagnosis was made. The entire abdomen was tense and markedly distended throughout all quadrants. Over the entire right side and left lower half of the abdomen no peristalsis was audible. The abdomen in this region was flat to precussion with relatively little tenderness but was uncomfortable, chiefly because of the terrific intra-abdominal tension that had built up over a period of about 7 days. No isolated masses could be felt and all of the bowel seemed to be displaced into the left upper

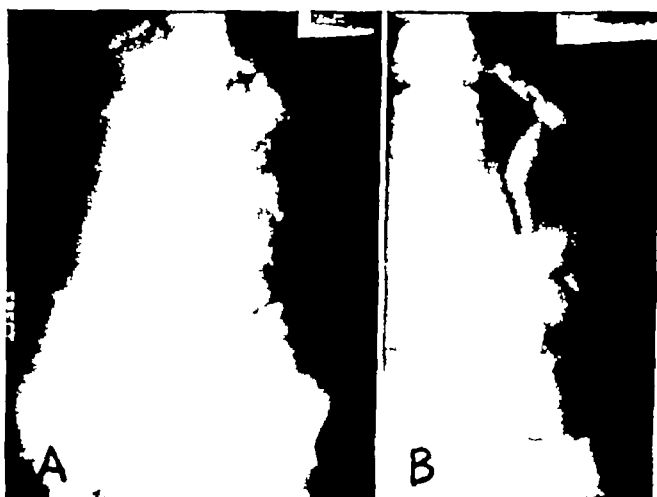


FIG 1 A excretory urogram showing no function or renal shadow on right side, and hydronephrotic double kidney on left side. Obstruction is at pelvic brim. Note absence of intestinal gas shown on right side of abdomen. B left hydronephrosis and hydro-ureter as shown in original excretory urogram.

quadrant. The patient was short of breath while recumbent because of the restricted diaphragm action. Because of the very rapid downhill course of the patient with progressive sepsis and finally the onset of obstructive jaundice with small clay colored stools, a second internist was called in consultation.

After completely reviewing the history and physical findings it was thought that the mass may well be retroperitoneal. An excretory urogram was extremely illuminating in that there was no kidney shadow or evidence of renal function on the right side, and the left kidney was a moderately hydronephrotic congenital double kidney with double hydro-ureters, both of which were compressed at the brim of the pelvis (fig. 1). On the day prior to her admission to the hospital her jaundice had deepened rapidly. The patient was comatose and the situation was indeed desperate. Marked nausea, vomiting and retching started with the onset of jaundice, and as the jaundice increased so did the gastrointestinal symptoms, which greatly aggravated the overall situation. At this point urological consultation was requested. The patient was first seen on the night of September 2, 1949.

Her general health had been good all her life except for a severe toxemia

On January 10 1950, employing sodium pentothal intratracheal ether and oxygen anesthesia, a left thoraco-abdominal nephrectomy was done. The line of incision was over the tenth rib and downward and across the abdomen. The tenth rib was resected subperiosteally near the spine. The diaphragm was opened in line with the incision. The renal vein and artery were dissected out and individually clamped and ligated. The ureter was isolated clamped and ligated. The kidney was then freed much of it by sharp dissection (fig 8). In the area of the renal pelvis an encapsulated perinephric abscess was found that burrowed into the psoas muscle. A stab wound was made in the flank and two rubber drains left in the renal fossa. The peritoneum was closed with interrupted sutures to cover the renal fossa and return the bowel to its normal position. Two Pezzer



FIG. 8. Case 4. Kidney bisected. Note scar tissue surrounding kidney.

catheters were left in the pleural cavity. The condition of patient was excellent throughout the procedure. She received 1000 cc of blood during the operation.

The postoperative course was uncomplicated except for moderate abdominal distention for the first 48 hours. Penicillin and streptomycin were given for the

first postoperative days and the highest temperature was 100.4 F. Seventy-two hours after surgery an x-ray of the chest revealed complete re-expansion of the lung and the Pezzer catheters were removed (fig 7 B). The rubber drains were removed on the seventh postoperative day. On the fifteenth postoperative day the patient was discharged with the incision healed and asymptomatic.

Her microscopic diagnosis was 1) chronic pyelonephritis with fibrosis, 2) chronic atrophy of renal pelvis and calyces, 3) adenoma of renal pelvis.

Case 5. M. L., a 50-year-old Negroess, was first seen January 19, 1950, with a history of abdominal indigestion of two months' duration with a dull aching pain in the upper abdomen.

2) partial left ureteral obstruction of undetermined etiology, 3) jaundice, probably obstructive in nature and of undetermined etiology

The retrograde study substantiated the left upper tract findings of the excretory urogram. The right ureteral catheter met an obstruction at the 15 cm level which could not be passed. The course of the right ureter was very abnormal in that the ureteral catheter curved abruptly crossing the midline so that its tip overlaid the left ureter as it crossed the brim of the pelvis. I was unable to force any contrast medium past the ureteral obstruction. See figure 3.

With this clue plus the excretory urographic findings, the patient was turned on her left side and the right flank over Petit's triangle was prepared as a sterile



Fig 3 A, displacement of right ureteral catheter with obstruction at 15 cm level. Note diffuse mass in entire right side of abdomen and pelvis. B, right side down oblique showing right ureteral catheter displaced posteriorly and overlying normal course of left ureteral catheter where it crosses brim of bony pelvis.

field. A No. 22 spinal needle was introduced through Petit's triangle 5 cm resulting in the free aspiration of thin pus. A diagnosis of pyonephrosis was made.

Under local anesthesia nephrostomy was performed and 9,000 cc of thin purulent fluid was recovered from the hydronephrotic sac. A No. 26 Malecot catheter was used as a nephrostomy tube with gravity drainage. Following this procedure her recovery was phenomenal. Within 36 hours she was afebrile and her sepsis and prostration had all but disappeared. The jaundice cleared in 4 days and she rapidly returned to a full diet. A postoperative chest film showed the right leaf of the diaphragm at its normal level.

In the interval between the nephrostomy and the nephrectomy a retrograde study was done on the left side and a normally functioning, uninfected, congenital double kidney was demonstrated. The previously noted left hydronephrosis and hydro-ureter had completely disappeared. There was a Y ureter with the bifurcation about one cm above the bladder. See figure 4.

A nephrostogram on the right showed a giant hydronephrosis which had shrunk over 50 per cent (4,000 cc) as a result of continuous nephrostomy.

and ligated. The cystic mass with the kidney was then removed with some difficulty. The renal fossa was drained through a stab wound in the flank. The peritoneum was closed with a few sutures to cover the raw area. The diaphragm was closed with interrupted sutures of silk. A Pezzer catheter was left in the pleural cavity through a stab wound in the eighth interspace. The patient experienced a mild degree of shock near the end of the operation but responded well to whole blood transfusions. In all, she received 1500 cc blood during the operation.

The entire postoperative course was uncomplicated. The temperature rose no higher than 99 SF during the first 72 hours after which it was normal. The lung had completely re-expanded by the third postoperative day and the Pezzer catheter in the pleural cavity was removed (fig 9 B). The rubber drains were removed on the fifth postoperative day and the patient was discharged on the thirteenth post-operative day with the incision well healed (fig 10).



FIG. 10. Healed wound.

The microscopic report was: huge renal cyst and perinephric hematoma with left kidney and normal spleen. There was no evidence of tumor.

CASE REPORT. A 48-year-old white woman was admitted to hospital July 28, 1970, with a history of occasional hematuria of 6 months' duration. Fifteen days prior to admission there was severe hematuria with many clots.

Physical examination revealed a very obese woman with a large irregular firm tender movable mass in the right upper abdomen and flank. There was slight pitting edema of feet and ankles.

Laboratory findings were within normal limits except for blood and pus count. The preoperative chest film was negative for metastases. The retrograde pyelogram showed a normal left kidney; on the right there was a pressure deformity of the pelvis with some dilatation and elongation of the calyces (fig. 11).

A diagnosis of right renal tumor was made.

Two days after admission, two days later there was pain in the right flank. Twelve hours following this the patient developed dyspnea and tachypnea with a fall in blood pressure. A diagnosis of pulmonary infarction was made. The patient was given 500 cc blood, oxygen, and other supportive therapy. At the time of surgical consultation she was given heparin and

The patient stood the nephrectomy well and made a rapid and uneventful recovery. She has been followed in the office for over a year and at the present time is enjoying the best of health with normal kidney function and a negative urine.

SUMMARY

This case combines not only an infected hydronephrosis of near record size with a rapidly progressive jaundice and intense sepsis, but has the confusing factors of a short duration of the present illness, no pertinent past history, a relatively normal urine, vague misleading and indefinite physical findings, with a rapid downhill course. Until the excretory urogram was done no diagnosis had been made despite the advanced progress of the disease. Until this valuable procedure focused attention on the kidneys, an exploratory laparotomy had been seriously contemplated by the referring physician, a move which would have spelled almost certain death for the patient. A diagnostic aspiration through Petit's triangle was as a last resort, but led to a quick and accurate diagnosis. Once all of the facets of this case were properly evaluated the treatment was obvious. An emergency nephrostomy, under local anesthesia, served to bring the patient back to relatively good health with a minimum of surgery. By the judicious use of the nephrostomy tube all the obvious contra-indications of the ultimate surgical correction were effectively forestalled. This decision was paramount under the circumstances. With the jaundice and the left hydronephrosis corrected and the infection reduced to a subclinical level she tolerated the interval nephrectomy well and her return to good health was only a matter of a few weeks.

CONCLUSION

This case was presented to further illustrate the pitfalls and dangers of giant hydronephrosis. Our shortcomings lie in our inability to make an early and accurate diagnosis. Once the diagnosis is made the treatment presents no problem. This diagnosis should always be considered in all undiagnosed cases of vague clinical and physical findings associated with progressive abdominal swelling.

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isolated clamped and ligated. The kidney was then freed and removed. The renal fossa was drained through a stab wound in the left flank. A few sutures were taken to cover the raw area with peritoneum and fix the bowel back in position. Through a stab wound in the anterior axillary line in the tenth interspace a Pezzer catheter was left in the pleural cavity. Patient tolerated the entire procedure well. She received 1000 cc blood during the operation.

The temperature was 101 F the first post operative day and normal by the third post-operative day. Abdominal distention was present for 48 hours but responded to the use of the Miller-Abbott tube with Wangenstein suction. The lung had re-expanded by the third postoperative day and the Pezzer catheter and rubber drain were removed (fig 11, B). The remainder of the course was uncomplicated and afebrile.

Deep x-ray therapy was started on the twelfth postoperative day and she was given a total of 2200 r units. When she was discharged, the incision was completely healed and the patient asymptomatic (fig. 12).

The microscopic diagnosis was clear cell carcinoma with chronic pyelonephritis.

The 6 patients whose cases have been reported have all recently been examined and except for one (case 6) were all in good health and free of complaints. In this case a subcutaneous abscess developed in the incision 9 weeks following discharge from the hospital. The patient was very obese and x-ray therapy was started on the twelfth postoperative day. We believe it interfered with healing, contributing to the development of the abscess. The chest x-rays of the tumor cases at the follow up examination were all negative for evidence of metastases.

SUMMARY

We have used the thoraco abdominal approach for 6 nephrectomies. Three were renal tumors (one with kyphosis and inklosis of the spine) a unilateral polycystic kidney, a large cyst of the kidney, and a densely adherent infected kidney.

It is our opinion that the thoraco-abdominal approach affords a better exposure in easier and more satisfactory operation with a decreased morbidity and mortality in large renal tumors and cysts, densely adherent kidneys, and adrenal tumors than can be obtained by either the lumbar or transperitoneal approach.

In the 6 thoracic abdominal operations there were no deaths, no major complications, pulmonary emboli, chest or peritoneal hemorrhage or infection. There was one minor complication, 1 case requiring one thoracentesis. The convalescence of all patients has been exceedingly smooth and they have not been troubled with postoperative chest or nerve pain.

We are of the opinion that the majority of renal and adrenal tumors should be treated by the thoraco-abdominal approach.

We are indebted to Dr. Charles Donald, thoracic surgeon, for his co-operation in the operation and treatment of these cases. The absence of any serious chest complications is due to his excellent technique and ability in performing the operation and in directing its postoperative care.

[illegible]

doses of 40 cc, or basalgel, in doses of 30 cc, after meals and at bedtime. For individual patients the dosages were varied slightly, as indicated by quantitative analyses of the 24 hour urinary output of phosphorus, calcium and creatinine. The patients followed a diet supplying approximately 1300 mg of phosphorus.

TABLE 1

Average results of numerous random examinations on 37 patients (22 males, 15 females, aged 10 to 59 years)

	BEFORE PROPHYLAXIS NO. OF PATIENTS	DURING PROPHYLAXIS NO. OF PATIENTS	AFTER PROPHYLAXIS (OR END OF STUDY) NO. OF PATIENTS
Pvuria present	29	27	15
Pyuria absent	8	10	22
Culture positive	31	24	14
Culture negative	5 (1 no record)	11 (2 no record)	21 (2 no record)
Acid urine	13	15	16
Alkaline urine	24	22	21
H ₂ dronephrosis right	8	7	7
H ₂ dronephrosis left	9	8	9
Normal blood protein	37	37	37
Abnormal blood protein	0	0	0
Normal blood calcium	35	35	35
Abnormal blood calcium	2	2	2
Normal blood phosphorus	35	35	35
Abnormal blood phosphorus	2	2	2
Normal alkaline phosphatase	34	32	28
Abnormal alkaline phosphatase	2 (1 no record)	1 (4 no record)	0 (9 no record)
Urine phosphorus 24 hours			
Under 300 mg	1	18	14
300-600	16	16	14
Over 600	20	3	6 (3 no record)
Urine calcium under 250	31	31	28
Urine calcium over 250	6	6	5 (4 no record)
Urine creatinine (normal)	37	35 (2 no record)	35 (2 no record)
Stone right kidney	17	15 (2 passed) (2 decreased) (0 new) (2 increased)	14 (1 new) (2 increased) (1 passed)
Stone left kidney	18	16 (2 passed) (1 decreased) (0 new) (2 increased) (These last figures ignore lapses in therapy and follow chronology only)	15 (2 new) (2 increased)

and 700 mg of calcium per day. Each was urged to maintain a daily fluid intake of approximately 3000 cc. Antimicrobial drugs and urologic measures were employed according to the usual indications.

All the selected patients followed the prophylaxis reasonably well, although the regimen was not strictly adhered to in every case and deviations were demonstrable on an objective basis. In fact, some of the deflections provided the most impressive exhibitions of the effectiveness of the program. The cases of patients

THE REMAINING KIDNEY AFTER NEPHRECTOMY FOR TUBERCULOSIS—A CASE OF GIGANTIC HYDRO-URETERO- NEPHROSIS 22 YEARS AFTER OPERATION

EMILIO DE LA PENA

Cases examined many years after nephrectomy for tuberculosis are not common. It is well known that a number of patients operated upon die some years later of generalized tuberculosis or of tuberculosis of the remaining kidney. As for those with no urinary symptoms and good general condition after nephrectomy they seldom return to the urologist for a check-up especially if years have elapsed since operation.

A number of authors have discussed the problem of the remaining kidney after nephrectomy for tuberculosis and F. E. Gibson of San Francisco has pointed out the importance of ureteral stenosis as a cause of hydronephrosis of the said kidney. It is a known fact that tuberculous cystitis causes changes in the bladder

and the intramural portion of the ureter which may be followed by ureteral strictures and ureteral backflow. The following case is reported because of the long time elapsed since nephrectomy and also because in spite of the huge hydronephrotic remaining kidney the patient's general condition is good, as shown by x-ray examinations carried out in 1940 and 1949.

CASE REPORT

Mr. F. G. C. was a white woman 45 years of age. When examined by me in 1940 she stated that her left kidney was removed in 1927 because of tuberculosis. She now complained of attacks of slight fever with occasional discomfort on the right loin. At that time urinalysis showed moderate pyuria and B. coli with normal blood urea. An x-ray taken after bladder distention with opaque medium

similar to the one depicted in figure 1 taken when last examined. The patient returned to Argentina where she was living. Judging from the bad condition of her kidney I had the impression that she was not to live long. To my great surprise she has come again to Spain so that I have been able to examine her again. She now states that she has kept in good condition during these 9 years except for occasional attacks of fever with high blood urea which subsided under treatment with streptomycin. Her urine is pale and slightly cloudy. Her blood urea is normal. She only complains of slight discomfort on her right loin.

At operation with the bladder distended with opaque medium (fig. 1) a grossly dilated kidney with the ureter greatly dilated and filled with opaque medium was introduced in the bladder. In trying to fill the bladder at exposure it is noticed that only a small amount of opaque medium enters but after exerting some pressure on the kidney by palpation the whole amount of opaque medium was recorded.

SUMMARY

A case of hydronephrosis of the remaining kidney 22 years after nephrectomy for tuberculosis. The x-ray examinations

The fourth operation, a pyelolithotomy, was performed on a 39 year old woman because of impaired renal function. The residual calculus had not enlarged during the 12 month treatment period.

Twinn³ found a 24.2 per cent recurrence of renal calculi after lithotomy, and that 30 per cent of kidneys containing multiple calculi had recurrence. Oppenheimer⁴ found that 24 per cent had recurrence after pyelolithotomy and 58 per cent after nephrolithotomy, in a group followed for an average of 4 years, the same time interval as in our therapeutic series.

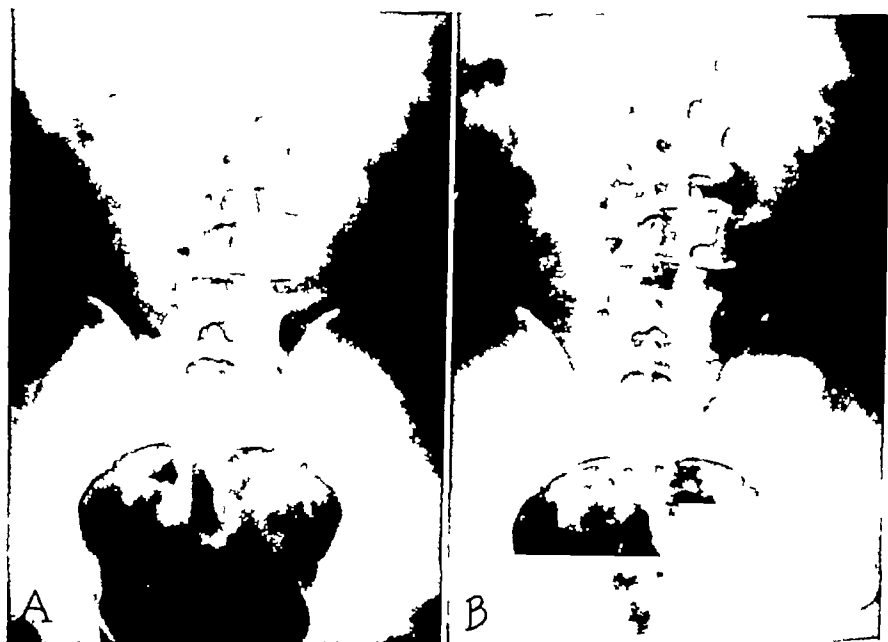


FIG. 1. A, no calculi after three lithotomies followed by 18 months on Shorr's regimen. B, recurrence within 9 months when patient discontinued therapy.

Thirty-three per cent of the grossly infected kidneys had recurrence and 14.6 per cent of those with originally unilateral disease had stone formation in the opposite kidney in the same period. Oppenheimer⁴ decided that 14.9 per cent of the pyelolithotomies and 29.4 per cent of the nephrolithotomies clearly had recurrence of new calculi exclusive of growing residuals. Twinn records that 35 per cent of the renal phosphatic calculi recurred. Accordingly it would be reasonable to expect a 25 to 35 per cent recurrence in our particular series. This indicates that 9 to 13 in our group would likely have had a recurrence, and possibly a few would have formed a calculus in the previously uninvolved kidney.

No new stones developed in any patient of this series while on the prophylactic regimen, yet all were known to have formed renal phosphatic calculi naturally. In fact, all but five were known to have formed more than one calculus.

³ Twinn, F. P. A study of recurrence following operations for nephrolithiasis. *J. Urol.* 37:259-267, 1937.

⁴ Oppenheimer, G. D. Nephrectomy versus conservative operation in unilateral calculus disease of the upper urinary tract. *Surg. Gynec. & Obst.*, 65:329-336, 1917.

DUODENAL INJURY IN RIGHT RENAL SURGERY

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The second portion of the duodenum is normally contiguous to the right renal mass and pedicle, separated from these structures by the thin anterior layer of perirenal fascia and the perirenal fat. Under certain conditions, however, these partitions may be obliterated so that the extraperitoneal descending portion of the duodenum will be adherent to the surface of the kidney or the pedicle. When this situation exists, the danger of injury to the duodenum during right renal surgery is increased tremendously.

Mayo¹ in 1914 was the first to call attention to this accident. At that time, he was unable to find any previous description or case report of this untoward complication. He believed that this injury most commonly occurred in those cases in which adhesions between the kidney and duodenum resulted from previous right renal surgery or inflammatory disease.

He stated that injury occurred as a result of direct trauma to the retroperitoneal section of the duodenum in application of the pedicle clamp, especially when hastily or carelessly applied during brisk hemorrhage.

Other conditions which might result in duodenal trauma with resulting fistula are:

1) Erosion by pressure from packing, drains or tubes lying in contact with the duodenum.

2) Ulceration of the duodenum in roughly freeing up a "frozen" kidney.

3) Inadvertent stitch injury in repairing a tear in the adjacent peritoneum.

Mayo recommended a transperitoneal approach to the fistula, mobilizing the descending portion of the duodenum from its bed with primary suture of the opening followed by reinforcement of the closure with a flap of peritoneum or omentum and finally a jejunostomy for feeding purposes. In 3 cases he describes, all patients died within 2 weeks following onset of the fistula. None was treated surgically.

Oberblad and Gonzales² in 1935 reported 1 case and found 25 additional case reports in the literature. The overall mortality rate was 48 per cent. The 7 patients who survived conservative treatment healed spontaneously after draining varying periods of time from 7 days to 4 months. Of 11 patients treated surgically, 4 died, the 7 survivors being treated by various procedures, namely, 1) excision of the fistula, jejunostomy, or gastroenterostomy.

Schneider³ in his review of the results of treatment of 33 cases found in the literature concluded that there was no material difference in mortality rates of conservative treatment. In 19 cases treated conservatively, the mortality was 37 per cent; in 14 treated surgically, the mortality was 50 per cent. Schneider pointed out the importance of this difficult case.

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renal function but showed tiny calculi in both kidneys. Frequent studies revealed a steady increase in calculi and a progressive reduction in renal function, so that ultimately huge staghorn calculi were present in both kidneys and intravenous pyelography demonstrated no function up to ninety minutes (fig. 3, *B*). The patient was placed on the prophylactic regimen in April 1944 (nearly 4 years after the previous operation). The existing calculi ceased to enlarge and ac-

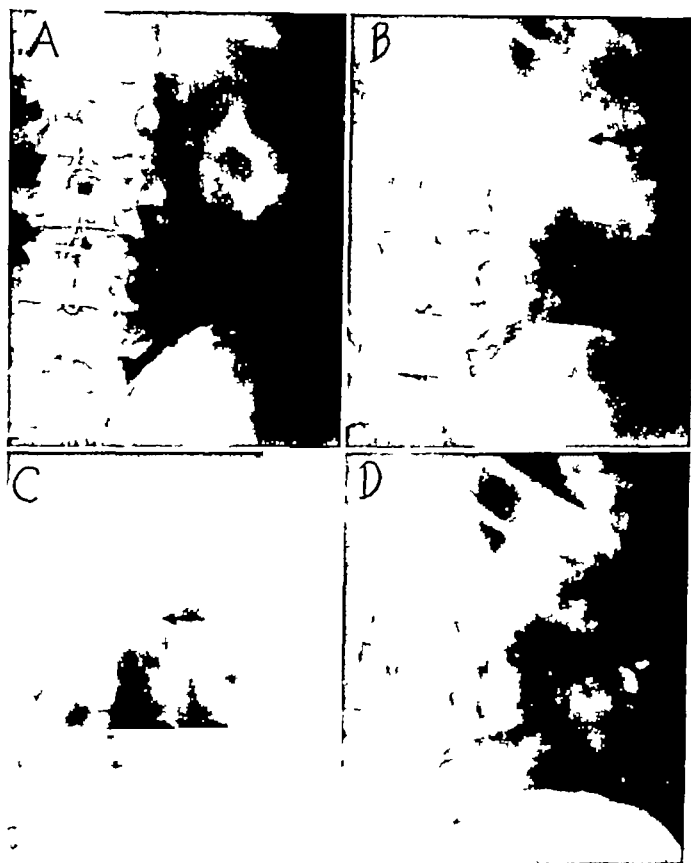


FIG. 2. *A*, recurrent staghorn calculus in solitary kidney after one lithotomy on that kidney but no specific prophylaxis. *B*, residual calculi enlarged. *C*, calculi unchanged after 11 months on Shorr's regimen. *D*, calculi enlarged over 7 months when patient discontinued therapy.

cordingly we were encouraged to remove the stones in the left kidney (March 1946, almost two years after beginning the prophylactic program). Because of infection and poor renal function, the postoperative course was stormy, and we decided against further surgery. The patient adhered faithfully to the regimen and in April 1950, four years after the last operation, roentgenograms (fig. 3, *C*) revealed some fragmentation of the large right staghorn calculus, with no evidence of recurrence on the left side. The 24 hour urinary phosphorus excretion averaged 250 mg. per day. The patient expired in uremia 52 months after the last operation and at autopsy the left kidney, although massively infected, was

and retrograde) were within normal limits, with the exception of a slight hydronephrosis of the right kidney and a kinking of the proximal right ureter. Neurosurgical and orthopedic clearances were obtained. *P. aeruginosa* was cultured from the right kidney urine.

On March 29, 1948 the right kidney was explored. The proximal ureter was discovered to be bound down by adhesions. A ureterolysis, renal sympathectomy and Denning type nephropexy were done and the patient was returned to the ward in good condition. The immediate postoperative course was uneventful.

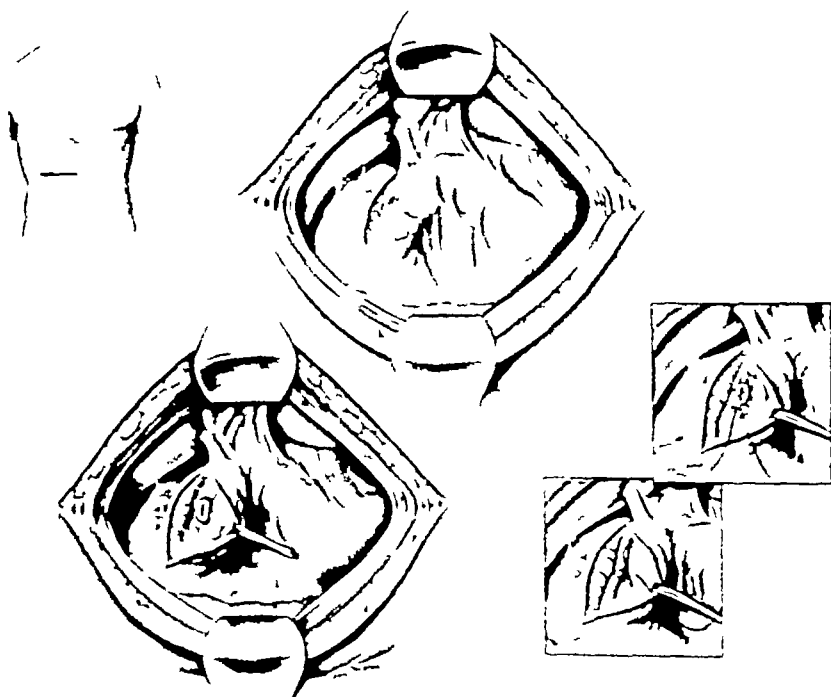


FIG. 1

The following day the patient's general condition was poor; he was markedly anorectic, the pulse was rapid, and the temperature elevated to 102.5°F. There was a profuse bile-stained drainage from the right flank wound.

That afternoon the patient was returned to the operating room and the abdomen was explored through a right upper anterior transverse incision (fig. 1). Upon entering the peritoneal cavity, a small amount of blood and bile-stained fluid were encountered. The descending portion of the duodenum was mobilized by turning its lateral peritoneal reflection, which was quite boggy and adherent. Perforation of the duodenum medially revealed a 1 cm. perforation posteriorly, which was closed with a 00000 atraumatic pure silk string. It was then closed with interrupted 000 silk Lembert sutures. The duodenum was returned to its normal position without re-suturing the lateral peritoneal reflection. The abdominal wound was closed in the usual manner.

method of preventing stone formation. Phosphatic encrustations on catheters, drains, ulcers and tumors exposed to infected urine are so common as to make additional comment unnecessary. Many measures have been suggested to aid in prevention of such encrustations for example, reduction of urinary infection, acidification of the urine, mechanical cleansing, and irrigation with certain practical solvents, like solution "G." We have found the gel-dietary regimen efficacious in preventing phosphatic encrustations. In many instances pre-existing soft encrustations have disappeared. Really hard and massive encrustations are seldom eliminated without additional measures and we do not imply that this program supersedes all others. Occasionally, change in composition of the urine seems to have a palliative effect, particularly on the symptoms of cystitis. These recurring impressions are difficult to confirm because details in individual cases vary markedly and objective signs are limited. Perhaps one example may convey the origin of these unproved ideas.

Mrs. A. O., N.Y.H. No. 569974, a 52 year old woman, invaded with urinary frequency, nocturia, urgency, hematuria and severe dysuria, was admitted for evaluation of a supposed extensive carcinoma of the bladder, which had been the diagnosis made elsewhere. Previously, the right kidney had been removed for calculus disease, the remaining kidney contained multiple stones. There was cystoscopic evidence of acute and chronic inflammation, blood oozed from several areas and the urine was grossly purulent. Repeated biopsies and review of the original biopsy failed to confirm the diagnosis of carcinoma. The patient had frequently passed small calculi and an analysis of one of these showed magnesium ammonium phosphate, calcium phosphate and calcium carbonate. Aureo-mycin and chlortamphenicol were administered and vesical irrigations performed for 15 days, and during this period the prophylaxis was instituted. In the 7 months since discharge the regimen has been carefully followed and no antimicrobial drugs have been administered. Urination occurs about every 2 hours during the day and twice at night (a reduction to well below half). There has been no gross hematuria, vesical discomfort varies but is markedly reduced, so that her son states "The improvement is nearly 100 per cent compared to a year ago." Signs of inflammation can be noted only by meticulous cystoscopic inspection. Pyuria persists. The improvement might be attributed to the brief course of antibiotics and vesical irrigations, but one can hardly ignore the implication that the gel-dietary program has been a major symptomatic aid, particularly since no other treatment has been administered in the ensuing 7 months in which the stones have been present and infection persisted.

DISCUSSION

Prolonged use of the gel-dietary therapy has produced no recognizable pathologic lesions (see case 6). Shorr and Carter² could demonstrate no significant undesirable metabolic effects. It is safe to assert that within the time limits involved in this study, which are of practical significance, no major difficulty developed which was directly attributable to the regimen. However, the prolonged application of any program requiring the consistent co-operation of the patient presents certain problems. Some patients tire of the monotonous bland

GIANT HYDRONEPHROSIS CAUSING CONTRALATERAL HYDRONEPHROSIS AND OBSTRUCTIVE JAUNDICE

WILLIAM RICHARD SMART

Giant hydronephrosis is relatively uncommon and represents only about 3 per cent of all the reported hydronephroses. By definition any hydronephrosis containing 1000 or more cubic centimeters of fluid has been generally considered a giant hydronephrosis. After a diligent search of the available literature I was unable to find any case in which an hydronephrosis per se could be demonstrated as the etiological factor in causing both a contralateral hydronephrosis and an obstructive jaundice. In reviewing the literature the same pitfalls and deceptions as noted in this case were repeatedly cited and stressed by all authors: namely, 1) the insidious, vague, deceptive onset; 2) poorly localized pain and physical findings; 3) abdominal swelling (often late); 4) negative bladder urine in 60 to 70 per cent of cases; 5) usually misdiagnosed by the family doctor as ovarian cyst, gallbladder disease, ascites, cancer, perinephritic abscess, pyelonephritis, appendicitis, peritonitis (1 B) and visceral cysts of varying character; 6) diagnostic procedures often used are of grave consequence, such as paracentesis and laparotomy.

CASE REPORT

A 30-year-old white woman complained of pain off and on right flank 2 weeks' duration, progressive abdominal distention, 7 days' duration, and progressive jaundice and sepsis of 3 days' duration. She stated that she was in good health until 12 days ago (August 20, 1949) at which time she had a rather sudden onset of general malaise, chills, fever, fatigue and generalized aching. She felt as though she were catching the flu. All of these symptoms were progressing and her family doctor was notified. Her throat was inflamed and she had some discomfort in her right flank, but no colic or local tenderness. Her urinalysis showed a 1 plus albumin with an occasional white cell, but no red cells, bacteria or casts. A complete blood count showed 30 per cent monocytes and a diagnosis of acute mononucleosis was made on the basis of this. With rather vague and indefinite symptoms the patient was put to bed and given 600,000 units of penicillin in oil intramuscularly daily with 100 mg. of procaine penicillin every 4 hours. Her temperature ranged between 99 and 102 degrees. All of the signs and symptoms continued vague and seemed almost to subside until August 26, 1949 when on physical examination she was found to have a rather large cystic mass in the right lower quadrant which had not been detected on the original examination.

The mass was relatively nontender, could be poorly outlined and was not palpable from the pelvis. On gynecological consultation the next day the mass was found to be considerably larger and the patient was becoming more ill. She was given penicillin and all. On pelvic examination the mass was not palpable. On August 27, 1949, the patient was taken to the operating room for laparotomy. The mass was found to be a giant hydronephrosis. The contralateral hydronephrosis was also found. The obstructive jaundice was caused by the hydronephrosis. The patient recovered and was discharged on September 1, 1949.

large amounts will prevent formation of calculi on foreign bodies in the rat's bladder under conditions which in nearly all control animals resulted in development of stone. In addition they found an average decrease of 16 mg in the weight of pre-existing calculi when basaljel was added to the diet, in contrast to an average increase of 56 mg in the control group. However, over a four week treatment period pre-existing vesical calculi disappeared in only 4 of 32 rats.

Satterthwaite⁶ has reported that use of this regimen with postural drainage nearly eliminated formation of urinary calculi in a large group of paraplegics.

SUMMARY AND CONCLUSIONS

Thirty-seven selected patients were studied for an average period of 49 months for a clinical evaluation of the aluminum gel-dietary regimen recommended by Shorr for prevention of renal phosphatic calculi. Clinical, roentgenographic and chemical data were fairly complete in each case. Comparison of the clinical courses of these patients before institution of the regimen with their courses during the prophylactic program showed that the aluminum gel-dietary therapy drastically reduced stone formation. For instance, 78 operations for removal of calculi had been carried out before prophylaxis, but during the program only four were required and these for removal of stones which had been present before the start of the regimen or had developed following lapse in therapy.

Although the control data were not completely comparable with those of the study, the differences were marked and clearly at variance with common clinical experience in such cases. Five patients provided individual control studies by voluntarily discontinuing therapy, and in 3 of these calculi promptly recurred.

Certain other uses of the regimen have been suggested.

This study, which includes several of the cases reported by Shorr and Carter, further substantiates their clinical findings. The experimental work of Vermuelen and his associates and the clinical observations of Satterthwaite corroborate this study.

It should be emphasized that the cases here described were selected as a test of the program, that only phosphatic calculi are considered, that the dissolution of calculi was not the objective, and that the preventive program was carefully checked at frequent intervals. Several questions remain to be answered but the advantages of this prophylactic regimen appear far to outweigh the disadvantages.

⁶ Satterthwaite, R. W. Percy Jones General Hospital, Battle Creek, Mich. Read before the Section on Urology, Annual Clinical Congress of the American College of Surgeons, New York, Sept. 8-12, 1947, to be published.

with her first and only pregnancy 3 years prior to the onset of her present illness. Following delivery she had a rapid and uneventful recovery from her toxemia with checks of kidney and liver function done 1 month and 4 months post partum showing complete recovery of both organs. In the interval, she had been examined twice a year and had repeatedly negative urine examinations. She had never had any evidence of hematuria, pyuria or calculus. There had never been any renal colic nor had she had any associated gastro-intestinal symptoms with right flank pain or tenderness.

Temperature 103 F, pulse 110/min, respiration 22/min and somewhat labored. The blood pressure was 128/70 (right arm).

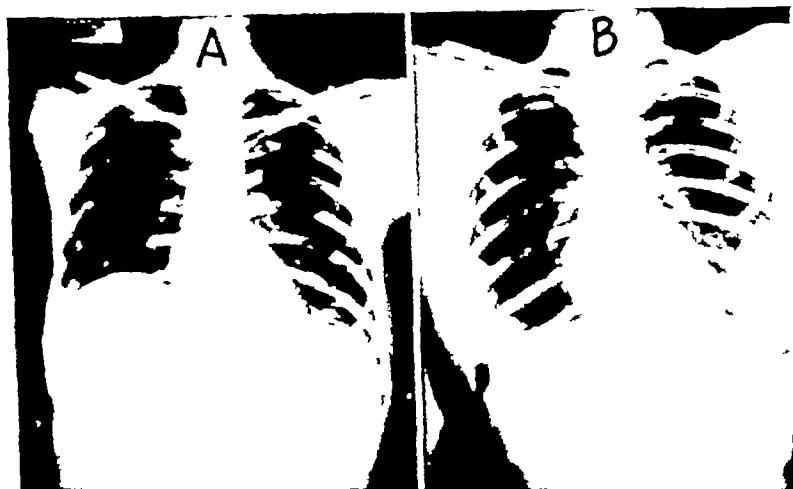


Fig. 2. A, chest film taken six days prior to nephrostomy. Note marked elevation of right hemidiaphragm, probably indicating marked pressure on liver and common bile duct with resultant elevation of diaphragm. B, chest film taken a few days after nephrostomy drainage had been established. Note normal level of right leaf of diaphragm.

The abdominal lumen was markedly distended and taut with fullness in both flanks. The skin of the abdominal lumen was stretched until it was shiny. The umbilicus was everted. On percussion dullness and flatness were the rule. The only peristalsis felt was in the left upper quadrant. First percussion in the flanks and costo-vertebral angle gave little response. There was no pitting edema in the flanks or in the abdominal lumen. The liver was not palpable. The right leaf of the diaphragm was at the level of the fourth rib anteriorly and was relatively fixed. It was not well substantiated with a chest x-ray preoperatively (fig. 2).

The left kidney is partially fixed and displaced downward as if there was pressure on it from above. No palpable masses were palpable.

Urine was 800 cc, specific gravity 1.028, 8 to 10 white blood cells, 8 to 10 red blood cells, 10 to 15 plus sugar, 4 plus no bacteria, pH 7.5. Bile 4 plus by Gram's method. Urine 100 cc, specific gravity 1.020, 6000 white blood cells, 10 to 15 red blood cells, 10 to 15 plus sugar, pH 7.5. Urine 100 cc, specific gravity 1.020, 6000 white blood cells, 10 to 15 red blood cells, 10 to 15 plus sugar, pH 7.5.

Urine 100 cc, specific gravity 1.020, 6000 white blood cells, 10 to 15 red blood cells, 10 to 15 plus sugar, pH 7.5.

inking that aluminum gel therapy was of major importance in the prevention of phosphatic calculi

(Slide) We have treated 31 patients with operations on the kidney for phosphatic calculi with aluminum hydroxide therapy since 1946. We have had one recurrence. Thus we can confirm the much more complete and detailed study by Drs. Green and Marshall.

(Slide) In groups 2, 3 and 4, we have treated a total of 107 patients. Here in group 4, we have tried to extend the use of aluminum gel therapy to those cases who have a) small renal calculi, b) small bilateral renal calculi, c) solitary kidney with small calculi, and d) those with renal calculi in whom operation may be contra-indicated. We have had some success and many failures.

In 2 cases in this group we have used topical irrigation with Suby's solution, followed by amphotel therapy, with complete success. This may be co-incidental. We are concentrating our efforts in group 4 at the present time.

In summary, while we believe that much additional work is yet to be done, we are of the opinion that the application of Dr. Shorr's original suggestions offers a simple and effective approach to the almost total elimination of phosphatic calculi in recumbent patients, and as so amply shown by Drs. Green and Marshall in their thorough study, provides for a marked reduction in the recurrence of phosphatic calculi in the operative patient. We believe that a close study of Drs. Green and Marshall's unabridged paper will fully justify their conclusions.

DR. VICTOR F. MARSHALL: I wish to emphasize that our 37 cases are a highly selected group not only as examples of ready formers of known phosphatic calculi, but most particularly as instances in which quantitative chemical analyses demonstrated objectively that the regimen was actually being followed. Quantitative studies are the only sure method of knowing that the program is in force. We omitted no cases in which we know the regimen was followed for at least a total of 14 months. The administrative details of the prophylactic therapy are omitted for brevity, not because they are unimportant. A large series and perhaps even long time intervals would be most valuable but considering that our cases were selected primarily as a test of Shorr's regimen, the present group seems to warrant this report today.

drainage for 4 weeks. At this time there was an incomplete obstruction clearly demonstrated low in the middle third of the right ureter. It is to be noted that at the time of the original retrograde study this was found to be a complete obstruction as a result of the intercurrent infection which accounted for the rapidity and severity of her illness.

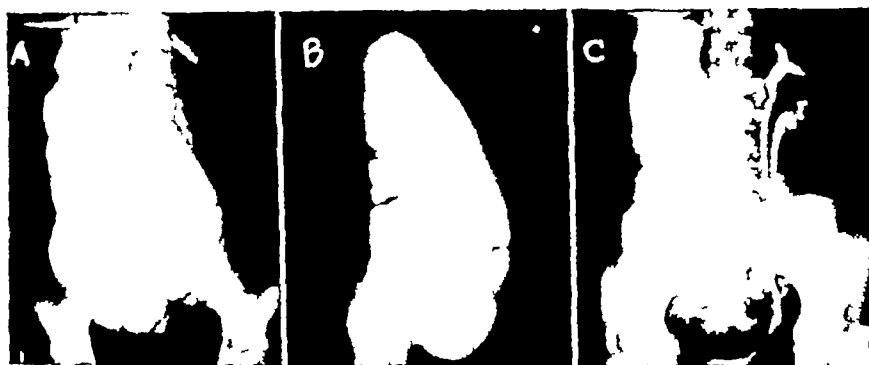


FIG. 4. *A*, first nephro-gram after nephrostomy showing giant hydronephrosis and contrast getting through to lower segment of right ureter. *B*, left side down oblique during first nephro-gram. *C*, following nephro-stomy and continuous drainage, right kidney has decreased in size with release of obstruction at pelvic brim; left hydronephrosis has subsided. Ureteral junction was found to be only a few centimeters proximal to bladder, on left.



therapy, followed by implantation of radon seeds, with resolution of the mass. Five months prior to admission, a mass developed on the left side of the neck for which similar therapy was instituted, again with a good response. At the time of her last visit to the clinic, 3 months before admission to Queens General Hospital, there was no sign of activity of the disease. It was one month later that she noted the onset of the symptoms for which she was admitted to Queens General Hospital.

The significant past history included exophthalmus since childhood and hyperthyroidism successfully treated with iodine 12 years prior to admission.

The physical examination revealed a chronically ill, pale woman with evidence of marked weight loss. The blood pressure was 140/85, the pulse rate was 40, respirations 16, and temperature 98.6 F. There was a right Horner's syndrome, and a small anterior cervical gland was felt on the right. The remainder of the examination was not remarkable. There were no palpable abdominal masses and no generalized adenopathy was present.

The laboratory findings included a blood urea nitrogen of 88 mg per cent with a creatinine of 5.6 mg per cent. The urine contained 3 plus albumin and many red and white cells, the specific gravity was 1.008. The red blood cell count was 3.9 million/cmm with 11 gm hemoglobin. The white cell count, serology, total protein and A/G ratio, BMR and electrocardiogram were all within normal limits.

The patient's hospital course was slowly downhill. She remained listless and vomited occasionally. After 6 weeks, the blood urea nitrogen had increased to 144 mg per cent and the creatinine to 10.8 mg per cent. The blood pressure rose to 160/100 mm Hg and the electrocardiogram now showed a left heart strain pattern. A chest x-ray showed findings consistent with cardiac decompensation. At this time a pericardial friction rub was heard. Despite parenteral fluids and an indwelling catheter, the urinary output remained small. Two months after admission, the patient lapsed into coma and died. The final clinical impression was carcinoma of the thyroid gland and uremia of undetermined etiology.

At gross autopsy, the significant lesions were found in the cervical region and in the kidneys. The neck, in the region of the thyroid gland, showed fibrous scarring. The thyroid gland was small and normal in appearance except for one small nodule in the right lobe which was firm, white, discrete and measured 1 cm in diameter. Below the thyroid on the right side there was a firm, white mass measuring 6 cm in diameter. This was adherent to the surrounding structures and its center contained the remnants of an anthracotic node. Just above the right lobe of the thyroid, there was a single lymph node 2 cm in diameter replaced by tumor similar to that of the infrathyroid mass.

Both kidneys were markedly enlarged with a combined weight of 1200 gm. The general contour and shape of the kidneys were preserved. On the external surface, through the capsule, most of the kidney was replaced by white tumor tissue. This fixed the capsule in several areas but did not penetrate beyond it as a perirenal tumor process. On stripping the capsule, the diffuse nature of the parenchymal involvement was obvious with a noteworthy absence of delimitation.

ALUMINUM GELS WITH CONSTANT PHOSPHORUS INTAKE FOR THE CONTROL OF RENAL PHOSPHATIC CALCULI

VICTOR F. MARSHALL AND JAMES I. GREEN

From The Department of Urology, The James Buchanan Brady Foundation of The New York Hospital-Cornell University Medical Center, New York, N. Y.

Shorr¹ in his original publication dealing with the prevention of urinary phosphatic calculi called attention to the potential value of the ability of aluminum gels to divert phosphate excretion to the intestinal route with a corresponding reduction in the amount excreted in the urine. In a later report on the therapeutic effectiveness of this regimen Shorr and Carter² described the dosage requirements for various aluminum gel preparations, the changes in serum phosphate levels associated with the reduced urinary excretion of phosphorus, as well as the adjunct dietary measures necessary to insure the optimal effects of this method of therapy.

This presentation is a review of the clinical results obtained by using Shorr's regimen for control of phosphatic renal calculi in 37 patients who had been selected because they showed a marked tendency to formation of renal phosphatic calculi under natural conditions, and in whom the tissue damage, obstruction and infection present in the urinary tract should have enhanced the rate of stone growth. Twelve patients had had unilateral nephrectomy (11 for calculi and one for tumor), so that the series included 62 kidneys. When the regimen was begun, 35 kidneys in 26 of these patients contained calculi, and in 11 patients the kidneys were stone free. Seventeen kidneys were hydronephrotic. All but 8 patients had pyuria.

For control the clinical courses of these same 37 patients before institution of prophylactic therapy were used, but we realize that this does not provide a completely reliable basis for comparison. Estimation of the time interval between detection of presence of stone and the institution of prophylaxis was difficult and probably inaccurate. However the best estimate based on *known* data was an average of 53 months; doubtless the interval was actually greater. As patients grew older the tendency to stone formation seems to diminish but we believe that this was of no significance in our study, considering the short time interval observed relative to the ages of the patients (which ranged from 10 to 59 years). Available preparations were fewer and less readily available during the preoperative control series, although in most cases sulfonamides and penicillin were used. Six patients had had nephrectomy, chloramphenicol and aureomycin as well as the aluminum gel. Of the 37 patients only 8 had no pyuria when the study was

interstitial fibrosis was also found in areas adjacent to tumor infiltrate. The tumor seemed to respect the kidney capsule though it penetrated it in isolated foci in the region of the larger vessels in the pelvis and in the region of the outer cortex.



FIG. 1. (A) section of thyroid gland showing diffuse infiltration of tumor cells ($\times 96$). (B) section of kidney showing massive replacement by tumor. Note that only remnant of renal parenchyma is a single glomerulus at periphery of the field ($\times 96$). (C) section of pancreas showing changes associated with uremia. Note marked dilatation of smaller ducts, many of which are filled with inspissated material ($\times 96$).

Some larger vessels were surrounded by tumor though not invaded. The vessels with the tumor in the parenchyma showed moderate sclerosis. All sections taken from areas of the kidney which grossly seemed least involved showed some tumor tissue.

Microscopically the pancreas (fig. 1 (C)) showed outstanding and remarkable

who had followed the regimen for less than a total of 14 months were excluded from this review, as they would not seem to provide a substantial test of therapeutic efficacy. The average total time on the program was 49 months. The longest continuous therapy was 92 months in 1 case. Two patients adhered to it for 90 months. These 37 cases were selected from a list of over 100 patients who had had an opportunity to follow the regimen for at least 14 months but who for various reasons, had not. At the same time, none were omitted who were known to have followed the program for 14 or more months.

The liability to recurrence or growth after lithotomy is recognized to be of vital significance. In this series, 78 operations (not including cystoscopic extractions) had been performed for removal of calculi before prophylaxis was instituted. However, during the average treatment period of 49 months, only 4 operations, on 3 patients, were done. In 2 patients the stone was present before prophylaxis was begun, and in the third patient two operations were necessary for removal of calculi which reappeared in both kidneys when he discontinued prophylaxis after following the regimen for 1 year.

CASE REPORTS

CASE I. J. J., NYH No. 288345, a 30 year old woman, was admitted with bilateral renal calculi. Hyperparathyroidism had been cured previously by removal of hyperplastic parathyroids. This was the only proved case of hyperparathyroidism in the present series. The prophylactic regimen was started, with biphosph 30 cc 4 times daily and a controlled phosphorus diet, after which the calculi in both kidneys ceased to enlarge but one moved into the right ureter, producing a hydronephrosis with infection. One year after the parathyroidectomy a right ureterolithotomy was carried out. In the subsequent 8 months the 24 hour urinary excretion of phosphorus has been maintained at 300 to 400 mg and there has been no change in the size of the remaining stone.

CASE II. D. C., NYH No. 281635, a 45 year old man, had repeated episodes of ureteral colic for 24 months. Radiography showed bilateral renal calculi and a right ureteral calculus. A right pyelolithotomy was done. The prophylactic regimen was instituted and 4 months later the patient passed two stones. Roentgenograms then showed a reduction in the number of stones remaining in both kidneys. The patient adhered to the regimen closely for 1 year and there was no change in the renal calculi. He then stopped both medication and diet. After 7 months without prophylaxis he passed a small stone, and in 28 months without prophylaxis the calculi in both kidneys had increased in size and several new stones had appeared. The prophylactic regimen was then resumed and a left ureterolithotomy was performed. After the calculus in the left kidney had entered the ureter, considering the left upper urinary tract free of stone. Five months after the ureterolithotomy a right pyelolithotomy, nephrolithotomy, and ureterolithotomy were carried out simultaneously. With the entire urinary tract now free of stones, the regimen was closely followed for 18 months and no further calculi appeared. The patient again discontinued therapy and within nine months a 1.5 cm calculus had appeared in the left kidney (fig. 1, p. 614).

filled lymph nodes is more likely. In our own series of 300 cases of uremia, this mechanism was responsible for 17 cases. It is possible to draw an analogy with impairment of hepatic function by metastatic tumor. In this latter instance, impairment is far more frequently the result of tumor obstruction of the biliary outflow tract rather than by actual replacement of hepatic parenchyma.⁷ Furthermore, there is a significant difference between the unit structure of the kidney as compared to the liver. Whereas the occlusion of a biliary radicle may destroy many liver cells, tubular obstruction in the renal cortex results in the destruction of only a few nephrons. Therefore, functional impairment occurs to a lesser extent in the kidney as a result of this mechanism. It is also apparent that death from progression of the tumor process usually occurs prior to replacement of sufficient renal parenchyma to produce uremia.

This entity should be considered clinically when uremia develops during the course of a malignant disease, particularly lymphosarcoma and leukemia, in the absence of a primary disease of the genito-urinary tract. The diagnosis is more likely if ureteral obstruction is ruled out by catheterization techniques and polycystic kidneys eliminated by radiographic studies. It may be of value to make this diagnosis, since radiation or nitrogen mustard therapy may improve the patient's renal status. However, this lesion occurs so infrequently that an accurate clinical diagnosis is indeed difficult.

SUMMARY

A case of uremia due to replacement of renal parenchyma by lymphosarcoma is reported. The literature relevant to this type of uremia is reviewed. Some reasons for the relative rarity of this entity are suggested. The diagnostic features and the clinical implications of this syndrome are discussed.

⁷ Kaplan, N. and Angrist, A. Surg., Gynec. & Obst., 77: 199, 1943.

In 3 kidneys residual stones became noticeably smaller during therapy, and 4 kidneys became stone-free by spontaneous passage of calculi. The one instance in which a stone seems to have dissolved is included with the latter four since it may have been passed asymptotically and since we feel certain that dissolution of well formed calculi by this regimen occurs rarely, if at all.

Case 3—A. B. N. Y. H. No. 410848, a woman aged 30 years, had had a right ureterolithotomy, and roentgenograms still showed bilateral renal calculi. She was then placed on the regimen and maintained it faithfully for 16 months. No stones were ever noted in the urine and at no time were there symptoms suggesting the passage of calculi, but during the last 8 months of this period the kidneys appeared by roentgenogram to be free of stone.

Case 4—I. M. N. Y. H. No. 513213, a 21 year old woman, had bilateral renal calculi and right ureteral calculus. On amphotel and the controlled phosphorus diet the 24 hour urinary phosphorus was maintained at less than 200 mg. After starting the regimen she passed all calculi and 12 months later was roentgenographically free of stone.

In 4 cases residual calculi did enlarge. The program for these patients was thoroughly reviewed and checked. Although a definite deflection in the regimen could not be demonstrated, it is probable that therapy temporarily lapsed since with subsequent adherence to the regimen there was no further increase in the size of the stones. This is illustrated by cases 2 and 5.

Case 5—S. I. N. Y. H. No. 380646, a 47 year old woman had had a right nephrectomy in 1940 at another hospital for "tumor of glomerular and tubular origin and questionable malignancy," a left pyelolithotomy in 1942 and a left nephrolithotomy for recurrent staghorn calculus in June 1944 (fig. 2 A). Residual calculi enlarged and 2 months later (August 1944) pyelonephrolithotomy was carried out. Again calculi returned. Prophylaxis was then begun and carefully followed for 34 months without change in the residual calculi. In the next 3 months the stones enlarged and the regimen was carefully reviewed (fig. 2 B). In the subsequent 11 month period there was no change (fig. 2 C). The patient then discontinued therapy and 7 months later the calculi by radiographic study showed an estimated 50 per cent enlargement (fig. 2 D).

Of the 35 kidneys containing calculi at the start of the program four became stone-free, three by passage or dissolution and one by operative removal. In 19 kidneys calculi decreased in size. In four kidneys residual stones temporarily enlarged. In 24 the calculi remained unchanged.

The favorable results obtained with this prophylaxis encouraged us to undertake treatment of phosphatic renal calculi from patients upon whom we would not have been a most reluctant to operate because prompt recurrence was

skin was pale and dry. Her temperature was 99 and the pulse was 112, blood pressure was 130/80. Laboratory findings: Hemoglobin 10.5, red blood cells 3.8, white blood cells 18,000, hematocrit 36 per cent, urinalysis negative, no red blood cells. The essential physical findings were dullness of the right base of the lung with diminished breath sounds, but no audible rales. The abdomen was tense and tender, especially in the upper right quadrant. There was a feeling of fullness in the right abdomen, extending almost three fourths of the way to the pelvis. Peristalsis was normal. The patient was treated conservatively for shock with supportive therapy. During the succeeding hospital days, the patient ran a



FIG 1

septic course and a definite mass became outlined in the right abdomen. X-ray studies revealed normal lung fields with a large ovoid shadow occupying the entire right quadrant of the abdomen, the shape of which suggested a retroperitoneal mass. Cystoscopy and pyelogram revealed that although the morphology of the mass was not characteristic of a renal tumor, there was evidence of pressure in the upper right calyx (fig. 1). This was thought to be due to a tumor of the upper pole of the kidney or possibly an extrarenal growth. After 13 hospital days of preparation, during which the temperature returned to normal and the clinical condition greatly improved, the patient was brought to surgery. The kidney was exposed through a lumbar incision. The upper pole of the right kidney was found to be replaced by a fleshy, friable mass approximately 4 times the normal size. The lower pole of the kidney was not affected. The mass encircled the adrenal gland and was fixed to the diaphragm and also to the inferior vena cava for approximately 12 cm. The twelfth rib was removed subperiosteally to aid in exposure and after first ligating the vascular pedicle

still stone free. Throughout the course in this case the urine was always grossly purulent on culture, *B. proteus* was most consistently found.

It is worthy of note that in this patient (case 6) there was no formation of stone while on the regimen despite persistent infection and marked tissue damage in the left kidney. Furthermore at least the last recurrence had taken place *after* the reduction in renal function. In other words, it is most difficult to attribute the final success of prophylaxis to a derangement of renal excretion which did not permit formation of calculi. Indeed, all evidence argues strongly that without prophylactic measures stone would have recurred. In case 7 after two previous operations without prophylaxis new stones promptly developed in the remaining kidney but a third removal followed by the prophylaxis has kept the patient stone free for over 5 years. Here again it is difficult to attribute success to a fortuitous change in renal function.

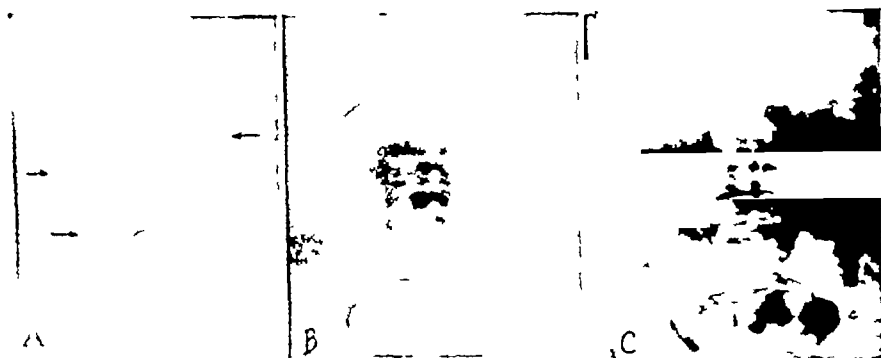


Fig. 7. A, bilateral calculi and right ureteral calculus. B, residual calculus increased to adult type. C, no recurrence of left calculus after complete nephrectomy and faithful adherence to regimen for 52 months.

Case 7. J. C. NYH No. 507003, a 37-year-old man, had had four operations including a left nephrectomy for removal of renal calculi. In March 1945 a complete nephrectomy was performed on the remaining kidney. Prophylaxis was then started and after 60 months of faithful adherence to the program the kidney (A) shown by roentgenogram contains no calculi.

Contrasting the foregoing case, patient A. K. (case 8), a 27-year-old woman, was stone free after a right pyelolithotomy. She was never on the prophylactic regimen. Within 12 months passed a large amount of gravel on numerous occasions. Roentgenograms 24 months after operation revealed a staghorn cal-

slight scoliosis to the right side and the psoas shadow was not distinctly marked on the left.

The impression was gained that the findings indicated the presence of a large mass in the left upper quadrant of the abdomen with a displacement of the diaphragm and bowel, and possibly the kidney. It was believed that this might represent a hematoma, a ruptured spleen or even, possibly, a ruptured kidney. The patient was treated conservatively with supportive therapy and brought to surgery on the third hospital day. The abdomen was explored through a left upper rectus incision and a large retroperitoneal mass was found on the left side. The lateral reflection of peritoneum was incised and a large amount of bloody fluid obtained. A biopsy of the mass revealed some degenerating tumor-like tissue with the gross appearance of a Wilms' tumor. Because of the tremendous mass which extended down from the diaphragm as far as one could reach and across the midline of the abdomen, it was considered advisable to close, and institute x-ray therapy before any further surgical procedure could be carried out. The pathological report was that of a Wilms' tumor. Grossly, the fragments of tissue were very friable with some hemorrhagic necrosis that had the gross appearance of sarcoma. Microscopically the growth was a very cellular one, mostly spindle in type with no definite arrangement. The patient had an uneventful postoperative course and 7 days postoperatively received a total of 1800 r.u. in divided doses of 600 r.u. to each field. The mass responded promptly to x-ray therapy and a definite shrinking in size was noted. An intramuscular urogram suggested the presence of intrarenal disease on the left side. Following the completion of the x-ray therapy, a transperitoneal nephrectomy was done. The tumor was isolated retroperitoneally and separated from the adrenal and the pancreas. The vessels were clamped and ligated and the mass was removed in toto. The cavity was drained retroperitoneally and closed in layers. Postoperatively the patient again had an uneventful course and was discharged from the hospital 15 days after the second operation. Further postoperative radiation was given in the Out-Patient Department. The latest chest film taken one month ago, 5 years after operation, revealed no evidence of metastasis.

DISCUSSION

These cases bring up several interesting problems which combine the question of renal trauma and pre-existing lesions of the kidney. As previously mentioned the kidneys are well protected from external force and in these cases the trauma was relatively minor. The cardinal symptom of severe renal trauma is usually hematuria, which appears shortly after an accident but which may be delayed for several hours, thus did not appear at all in these children.

Of course, complete laceration or even occlusion of a ureter may give an absence of hematuria, but here again, the exciting force was minimal. Both cases, evidently, appeared to be running the usual silent course which is common in Wilms' tumor. These children with Wilms' tumors have almost no symptoms referable to the urinary tract, and pain, anemia and weight loss are all rather late manifestations. The pressure symptoms of nausea, vomiting and constipation from the presence of the growth in the gastro-intestinal tract are also late

ne of the gel for these the addition of flavoring extracts has helped. A few have taken the medication on cereal. Occasionally a patient may prefer Imphojel in tablets to the fluid form. Taking liquid medicine regularly is inconvenient, but for this the old-fashioned hip flask has been found useful again. The expense to the patient is not great but over a period necessarily of many months, and even years, the cost does mount significantly for those in the lower income groups. Frequent visits to the physician, who will explain carefully the objectives of the program, go far in maintaining the patient's co-operation.

The two principal disadvantages are the tendency to constipation and difficulty of maintaining reasonable control of the regimen. An adequate fluid intake, occasional cathartics, and daily use of the laxative fruits and vegetables permitted in the diet have regulated bowel function satisfactorily in nearly all. A gel preparation containing magnesium trisilicate is particularly useful against constipation. Refractory bowel dysfunction is rare but may tax the physician's ingenuity. Although a few patients discontinued the regimen because of constipation we believe that for them this obstacle could have been overcome if we had been more solicitous and had been able to maintain co-operation longer.

Performance of control studies requires laboratory space, equipment, and personnel. It seems that any well-equipped establishment could readily make the necessary quantitative determinations of calcium, phosphorus, and creatinine on the 24-hour samples of urine. In rare instances unusual metabolic disturbances, such as hyperparathyroidism, are thus revealed, but analysis of the 24-hour urinary output for organic phosphorus is most important because it is the only reliable method by which to demonstrate that the program is actually being followed. Known or unknown to the patient. Occasionally dosage must be adjusted according to the results of the analysis.

What constitutes the borderline between satisfactory and unsatisfactory reduction in urinary phosphate has not been established. We arbitrarily sum to keep the 24-hour urinary output of phosphorus below 300 mg. In 34 patients this degree is maintained constantly at less than 600 mg. and in 18 of these below 300 mg. The question is to when it is safe to discontinue therapy cannot be answered; we suspect that patients who tend to form stones readily may have to stay on the regimen indefinitely.

TRANSURETHRAL ENDOVESICAL URETEROLITHOTOMY WITH THE RESECTOSCOPE

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The terminal or intramural portion of the ureter, which pursues an oblique course through the musculature of the bladder floor to terminate in the ureteral meatus at the corner of the trigone, is of both physiological and surgical importance. It is this relationship of the ureter to the bladder wall which is considered to be an important factor in preventing ureteral regurgitation during bladder distention. It is also this lowermost two or three centimeters of the ureter which has the most constricted lumen. For this reason, and other obvious reasons relating to inaccessibility, ureteral calculi impacted at this level present unusual difficulties.

Available endoscopic methods for removing calculi in this location include ureteral dilatation, indwelling ureteral catheter, manipulation with various special instruments such as the Howard cork-screw, the Johnson basket and the alligator forceps, and ureteral incision with the electrosurgical current to enlarge the ureteral meatus and thereby facilitate passage.¹ For a number of reasons, however, the usefulness of all of these methods is limited. Not infrequently it is impossible to by-pass the calculus with any type of instrument or bougie, or the operator may succeed only in upward displacement. Moreover, during instrumental manipulation, there is always the hazard that a surgical emergency may be created in case a calculus has been engaged which may neither be withdrawn nor released, to say nothing of the danger of ureteral injury resulting in urinary extravasation.

The open surgical removal of calculi impacted in the lowermost ureter involves either an extensive and deep, extraperitoneal, retrovesical dissection or a transvesical approach, the former of which often proves to be extremely difficult, while the latter is obviously objectionable. It is for these reasons that a more simple method comes to be particularly desirable.

The method, which we are about to describe, was presented independently by Ratner and Schneiderman in November 1950. They state that they first used the technique in January 1949.* The endovesical technique which we are presenting is applicable only in those instances in which the calculus occupies a sufficiently low position to produce an intravesical bulge of the so-called "roof" of the intramural portion of the ureter, which is clearly visible by cystoscopic inspection. The relationship of this bulge to the ureteral orifice is shown in figure 1. Without cystoscopic examination, however, one may be reasonably certain of

Read at annual meeting American Urological Association, Chicago, Ill., May 23, 1951.

¹ Coppridge, W. M., Roberts, J. C. and Rosser, R. G., Jr. Direct manipulation of ureteral stones through the urethra. *J. Urol.* 61:418-419, 1948.

* Ratner, M. and Schneiderman, C. Transurethral ureterolithotomy. *Canad. Med. Ass. J.* 63:153-157, 1950.

DISCUSSION

Dr. RICHARD W. SATTERTHWAITE (Ancon Canal Zone) It is a privilege to discuss this thorough and stimulating paper by Drs. Marshall and Green based on the original suggestions of Dr. Shorr. We believe that Dr. Marshall and Green's work is well documented with long periods of careful observation, detailed and multiplex chemical analyses and demonstrates clearly how recurrences of phosphatic calculi can be prevented.

Our own interest in the treatment of phosphatic calculi began in late 1945 when we had an opportunity for the first time to study Dr. Shorr's suggestions. I felt that this work was based on simple basic physiology and that the possibility of using the aluminum gels to produce a so-called phosphorus shunt in the body in order to eliminate the major building block of phosphatic calculi offered a new, untried and well worthwhile clinical study.

Within a few weeks I had more than two hundred paraplegic patients and other battle casualties in whom the incidence of phosphatic calculi was high under my observation at the Percy Jones Army Hospital. Since my change would be for the better, we began at once to use imphojel therapy combined with postural drainage to prevent and treat phosphatic calculi in a small series of these patients.

We reported our initial results on the use of the phosphorus shunt from kidney to bowel at the panel discussion at the American College of Surgeons meeting in 1947 of which Dr. Charles Higgins was the moderator. It might well have appeared that our enthusiasm for Dr. Shorr's original contribution was excessive. We can state again that this is the oral medication which materially alters the recurrence and possibly the treatment of phosphatic calculi as a whole.

Still in the short term recumbent patient with an abnormal urinary tract, with a high calcium and phosphorus output in the urine, aluminum gel and a low calcium and phosphorus diet are used plus the general measures of postural drainage, high fluid intake and antibiotics. This simple therapy virtually eliminates the occurrence of the so-called calculi of recumbency in this group.

resectoscope loop. Any bleeding from the edge of the ureteral wall may then easily be controlled with the coagulating current. In cases of unusually low location of the calculus the slice of tissue may include the ureteral orifice. Urethral retention catheter drainage for two or three days is then advisable, also bladder irrigations and the administration of sulfadiazine and penicillin to minimize the infection hazard. These patients may ordinarily be dismissed on the fourth postoperative day.

This method has been employed during the past six years in twenty carefully selected patients without serious complication and with uniformly satisfactory results. Although there is obviously no purpose in submitting each detailed case history, a brief combined summary of the records of the last three patients under recent observation is not out of place. Of these 3 patients (one female and two males, aged 58, 67, and 51) each gave a history of cystitic symptoms and recurrent unilateral flank pain in a ureteral distribution dating back over a period of from 4 to 9 months. One had chills and fever before admission. In each instance ureteral catheters and instruments met with obstruction at the 1 or 2 cm level. X-ray study aiding in the diagnosis of ureteral calculus is shown in figure 3. These three patients were dismissed on the second, third and fifth postoperative days respectively. Convalescence in each case was uneventful, the maximum temperature reactions being 100, 99.5 and 99.2F respectively. Upon follow-up examination in each instance it was possible to introduce a 10F ureteral catheter into either the normal meatus or the newly created opening made for the removal of the calculus. Figure 4 shows the ureterostomy at the time of the follow-up examination, also its relationship to the normal meatus.

COMMENT

Evaluating the methods of treatment for calculi impacted in the intramural portion of the ureter the method described appears to have many advantages over the methods in common usage because of its simplicity, safety, short period of hospitalization, and satisfactory end result, and particularly by reason of the avoidance either of a major surgical procedure or its alternative that is the tedious period of weeks of intermittent suffering, incapacity and uncertainty associated with awaiting spontaneous passage.

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UREMIA DUE TO REPLACEMENT OF RENAL PARENCHYMA BY TUMOR

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Uremia due to replacement of renal parenchyma by tumor is extremely rare. In 8467 consecutive autopsies performed at the Queens General Hospital from January 1936 through September 1950 there were 300 cases with uremia. Of these, only one was attributed to tumor replacing the renal parenchyma.

In 1941 Abshouse and Goldstein¹ collected 1458 cases of metastatic malignant tumors of the kidney from the literature and added 23 cases of their own. They pointed out that in no case was the diagnosis made antemortem and concluded that metastatic nodules in the kidney rarely, if ever, cause renal insufficiency. Old and Popp² reported three cases of lymphoblastoma with signs of renal disease which were improved by roentgen therapy. None of these was autopsied.

In 1946 Kretschmer³ collected 77 cases of bilateral renal tumors from the literature. Thirty-eight were sarcomas, of which two died with uremia, one case is reported in detail by Kretschmer in which 98 per cent of the kidney parenchyma was estimated to be replaced. The remaining 39 cases included four instances of uremia, two of which had undergone nephrectomy for a primary tumor in one kidney. Reichfeldt⁴ reported one additional case of lymphosarcoma in which renal insufficiency was present. There was extensive tumor replacement of the kidney parenchyma at autopsy.

In Merrill and Jackson's⁵ series of 18 autopsied cases of leukemia, ten had diminished renal function and four of these died with uremia. Three of the four cases had renal calculi. The authors concluded that renal failure in cases of leukemia may be due to renal calculi, leukemic infiltration, obstruction of renal pelvis or ureters by leukemic tissue, or to non-leukemic degenerative lesions of the kidneys.

We have since been unable to find any additional cases in the available literature.

The following are the reports of uremia due to replacement of renal tissue by

THE PHYSIOLOGY OF THE URETERO-INTESTINAL ANASTOMOSIS I URETERAL REFLUX

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From the Department of Surgery of the University of Chicago, Chicago, Ill

Radical surgery for early cancer of the bladder has been impeded greatly due to the fact that a large percentage of patients develop serious renal disease following the diversion of the urinary stream associated with the procedure. A successful uretero-intestinal anastomosis would obviate the understandable reluctance to early radical surgery for a disease which permits so little of conservative therapy. With more than 60 techniques for uretero-intestinal anastomosis already described in the literature it would appear that the cause of the frequent unsatisfactory results may not depend *per se* on the method used but on other more fundamental factors. It has long been considered that stricture formation secondary to the normal healing process at the site of anastomosis has been responsible for the hydro-ureter, hydronephrosis, pyelonephritis and uremia so often observed. A method to minimize this inherent defect by direct mucosal anastomosis has been proposed by Nesbit. It is the objective of the present study to point out that fibrosis and the resulting stricture are not sole contributors to this distressing problem. Ureterorenal reflux and ureteral neuromuscular imbalance appear to warrant consideration. This communication is concerned with the study of ureteral reflux while the subject of a subsequent investigation will be ureteral action potentials.

METHODS AND RESULTS

Seven patients were studied who had previously undergone uretero-sigmoidostomy. The procedure consisted of determining for each patient the average volume of urine normally "voided." A solution of 7 per cent sodium iodide was then introduced slowly into the rectum and an x-ray film taken following instillation of each 50 cc until the patient had a desire to "void." In the group of subjects examined the volume of urine normally necessary to produce the defecation reflex was found to be approximately equal to the amount of instilled contrast material which produced the same reflex. Using this technique, five of the seven patients had definite evidence of ureteral reflux. Two of these five cases had Nesbit direct mucosal anastomoses and the other three a modified Coffey procedure. In each instance regurgitation occurred with an amount of contrast material in the rectum considerably less than that necessary to initiate normal "voiding" (figs. 1 and 2). The intrinsic defect involved the absence of the normal ureterovesical valve thus permitting retrograde flow of the contrast material. In addition, the minimum volume of urine necessary to set-off the emptying reflex was so great it produced ureterorenal regurgitation before evacuation occurred.

It now became of importance to determine whether an ideally constructed

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This study was aided by the American Cancer Society Institutional Grant.

of tumor tissue. A more marked isolated and delimited rounded involvement in some loci was suggested. All areas of involvement merged into the adjacent parenchyma. The tumor tissue was whitish, very finely granular, relatively soft, and homogeneous throughout, bulging above the cut surface rather remarkably, as if under tension. Though involving the kidneys diffusely, the involvement seemed more marked in the region of the cortex. No streaked abscesses were noted. No purulent foci were discerned. Some necrotic areas were noted toward the medulla and several were pyramidal in shape. The pelves showed only slight dilatation and there were some areas of congestion and of hemorrhage noted. The ureters were not dilated and were thin walled.

Microscopically, the residual thyroid tissue (fig. 1, A) showed an increased fibrosis and lobulation with some adenomatous nodules containing more colloid. In the thyroid diffuse tumor tissue was found, consisting of hypertrophic pyknotic variable mainly rounded tumor cells. No alveolar or glandular pattern was present. The tumor was cellular and involved the thyroid regional tissue diffusely though showing some tendency to extend along trabeculae. Some vessels included in the tumor tissue showed diffuse invasion up to the intimal endothelium but not beyond. In one area a suggestion of rarefaction by larger more vacuolar cells was mindful of a Hickman center.

The infrathyroid tumor showed an alveolar massing of hypertrophic pyknotic hyperchromatic cells with considerable cytological variation in the nuclei and abundant cytoplasm. Some multinucleated giant cells were present though small. The alveolar arrangement was determined by a pronounced coarse hyaline reticulation. The tumor tissue extended through the capsule like structure diffusely and into the adjacent fat. Some well formed nerve structures were embedded in tumor tissue.

Sections of the kidneys (fig. 1, B) showed extensive involvement with identical pyknotic hyperchromatic and hypertrophic variable cells, more often rounded than occasionally elongated. Mitotic figures were frequent, many were atypical. Most of the tumor tissue was found in the interstitial stroma though some seemed to replace tubular tissue in situ with preservation of the basement reticulum of the renal tubules. Some tubules were well preserved, others showed distinct atrophy. No evidence of focal pyelonephritic suppuration was present. In some areas of

according to the method of Huggins. This consisted in the following: 1) A proximal colostomy was performed to defunctionalize the distal loop of rectosigmoid. 2) At a later operation the bladder neck was ligated and divided and finally the bladder anastomosed to the rectum. Ureteral urine passed directly through the bladder into the clean rectum. The function of the colostomy was to reduce to a minimum one more variable in the problem, namely, that of infection from fecal contaminated urine. Ten such dogs were studied. Twelve to nineteen months following vesicorectal anastomosis cystorectograms were performed on four dogs. The same procedure was used as previously described for humans. In three dogs ureteral reflux was radiographically observed with an amount of contrast fluid which was considerably less than the volume necessary to initiate the rectal

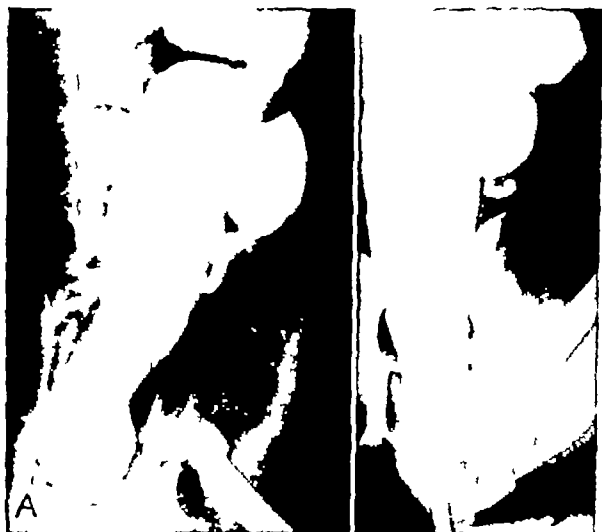


FIG. 3. A. dog 446. Vesicorectal anastomosis. Eight months postoperative. Normal voiding 400-500 cc. Cystorectogram using 200 cc sodium iodide demonstrating incompetence of ureterovesical valve and ureteral reflux.

B. dog 693. Vesicorectal anastomosis. Nineteen months postoperative. Normal voiding 250-300 cc. Cystorectogram using 100 cc sodium iodide demonstrating incompetence of ureterovesical valve and ureteral reflux.

defecating reflex (fig. 3). In the fourth dog an inconclusive study was made. The volume of intracolonic urine necessary to set-off the reflex apparently exerts too great a pressure on the normal ureterovesical junction resulting in incompetence of the valve.

Six dogs died of renal disease and three dogs were sacrificed. Autopsy was performed on the nine animals and each had hydro-ureter, hydronephrosis, pyelonephritis and several had renal calculi. The one remaining live dog has passed a calculus per rectum. Sections for histologic examination were obtained from each kidney and each ureterovesical junction. Several dogs had formed a small papilloma at the site of the ureteral valve. This was composed of dense fibrous tissue. The diagnosis of advanced, diffuse pyelonephritis was confirmed microscopically. The ureterovesical junction revealed incompetence of the valve and an increase in fibrous tissue deposition about the intravesical ureter and adjacent

minature cystic dilatation of the smaller duct structures described in uremia. An occasional large one was also filled with inspissated eosinophilic homogeneous material. Fibrosis was present isolating a lobular pattern. The islets were intact.

The final pathological diagnosis was lymphosarcoma involving the thyroid gland and cervical lymph nodes with massive replacement of both kidneys and resultant uremia.

DISCUSSION

Despite massive involvement by tumor tissue it may be possible that another factor was contributory to the development of the uremia. Pyelonephritis, however, was not present. Nephrosclerosis was not severe enough to account for the clinical findings. Necrosis in tumor and kidney parenchyma was present probably secondary to vascular occlusion due to tumor with resultant infarction. In the region of the pelvis, areas suggestive of papillary necrosis similar to that occurring in devitalized states in cases of far advanced malignancy were present in the gross, but microscopic study showed only minute areas of such involvement. The hyaline material seen in the stroma suggested amyloidosis but the glomeruli were uninvolved. If any of these mechanisms applied in this instance they were obscured by extensive and diffuse tumor invasion. The primary role in the pathogenesis of the disordered renal physiology must be ascribed to the massive tumor infiltration of both kidneys.

It is not surprising that the original pathological diagnosis of the thyroid biopsy was interpreted as anaplastic carcinoma in view of the morphological similarity of anaplastic carcinoma and lymphosarcoma. The anatomical distribution, gross and histological appearance with a suggestive follicular pattern in some areas, and the behavior of the tumor in response to radiation therapy—all favor lymphosarcoma as the most probable diagnosis.

It has been demonstrated by Abeshouse and Goldstein that the incidence of renal metastases in malignant disease is 5.1 per cent. The reason for this relative rarity is not known. These authors further point out that proportionately sarcomas metastasize to the kidneys more frequently than carcinomas. This may be attributed to the tendency of sarcomas to spread via a hematogenous route in contrast to the more frequent lymphogenous spread of carcinomas since it is well known that most metastases to the kidney are blood borne. Willis¹ has stated that although the cortex is usually involved first because of its accessibility, the glomeruli are the components most resistant to tumor

Reflux may occur when two conditions obtain first, a patent ureteral stoma must be present and second, intracolonic pressure must exceed intra-ureteral pressure. In the cases studied it appears that the pressure within the colon exceeds that within the ureter before the defecation reflex is initiated. From our observations should the patient experience the desire to "void" he probably already has ureterorenal reflux. The value of frequent "voidings" is obvious. The rectograms presented are of resting pressures which does not take under consideration the known fact that intracolonic pressure is elevated 100 per cent during evacuation. Were this latter aspect investigated it would unquestionably reveal reflux of a greater degree than during resting periods.

An additional factor must necessarily be considered. Following any of the accepted techniques of uretero-intestinal implantation a certain percentage of patients will have normal upper urinary tracts. Graves has noted that most patients falling in this category have nonmalignant disease. Our experience has been nearly identical. It is interesting to observe that preoperative pyelograms were normal in all patients having normal postoperative films irrespective of diagnosis. In these patients the crux of the explanation may depend largely on the preoperative physiological status of the ureter. This concept is not new. Braasch in 1913 cut the ureterovesical valve in normal dogs and found that reflux did not occur in most instances. He concluded that the check-valve action of the intravesical ureter is of contributory rather than paramount importance. In the absence of the valve, reflux may be prevented by the the normal physiologic function of the ureter which compensates for the loss.

An attempt has been made to demonstrate experimentally that should it be technically possible in the future to construct a physiologically normal uretero-intestinal valve, the persistently elevated intracolonic pressure would ultimately break down the competency of this valve. As a result of this incompetency 100 per cent of the dogs studied had renal disease and 60 per cent died within 19 months. Infection would undoubtedly hasten the process. A comparable phenomenon is observed frequently in humans with long-standing increased intravesical pressure secondary to benign prostatic hypertrophy. The breakdown of the mechanical action of the valve following infection is often present in tuberculous cystitis or nonspecific cystitis of the paraplegic patient.

As a result of these observations it would appear that the method which minimizes the evils of fibrosis and also reflux is use of the direct mucosal technique but with implantation of the ureters in the mid-descending colon instead of sigmoid. At this level the greater volume of urine is carried from the patent ureteral stoma into the generous reservoir below. Rectal evacuation would occur before urine reached the anastomosis. Observations of a few patients so treated indicate this to be the case. In addition, recommendations should be given the patient to "void" more frequently than the physiological urge demands.

CONCLUSIONS

Ureterorenal reflux of fecal contaminated urine occurs in some patients following uretero-intestinal anastomosis.

SURGICAL CORRECTION OF FEMALE STRESS INCONTINENCE

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Female stress incontinence has long been recognized as a clinical entity but there have been no satisfactory explanations of the cause or mechanism of this condition. Treatment, therefore, has been largely on an empirical basis. In this communication the anatomical factors accompanying female stress incontinence will be demonstrated and the mechanism of such urinary leakage presented. Operative technique will be discussed and results evaluated in a series of 15 patients recently treated.

ANATOMY AND MECHANISM

The base of the female urinary bladder and urethra are held in position by definite fascial structures of the superior layer of the pelvic diaphragm (fig. 1). This layer of endopelvic fascia is attached laterally to the arcus tendineus of the pelvis, and forms the superior covering of the levator ani muscles. The fascia, with the levator muscles, dips downward and medially from each side like a pair of hands, uniting in a median raphe. The raphe extends from the pubic symphysis to the tip of the coccyx and is pierced in the female by vagina and rectum. Anteriorly, in the wedge between the pubic bones, it merges with the superior layer of the triangular ligament and is pierced by the urethra.

This superior layer of pelvic diaphragmatic fascia forms a hammock like support to the base and neck of the bladder, and this specific portion has been termed "pubo-vesico-cervical fascia." This structure is the chief support of the urethra and bladder base, when it is torn or weakened ptosis of the vesical neck occurs (fig. 2). These conditions are sometimes met after childbirth and after the menopause, when general fascial relaxation may develop. Stress incontinence is always accompanied by a ptosis of the vesical neck. On the other hand the normal bladder never exhibits such mobility during stress, but remains in the shape of an oblate spheroid, becoming slightly flattened with the neck descending no more than $\frac{1}{2}$ inch.

It appears that the sphincter musculature alone is not capable of keeping the urethra closed during periods of great intravesical pressure and that normally it is assisted by the support and pressure of the pubo-vesico-cervical fascia. It can be shown by oblique or lateral cystograms taken while a patient with stress incontinence is straining, that a wedge of dye enters the proximal urethra even before urinary leakage occurs (fig. 3). From the physical laws of pressure one can readily understand why such a sphincteric mechanism could not remain closed. The hydraulic wedge effect causes pressure to be applied over a relatively large area on the inner aspect of the sphincter muscle, so that the total force available to open the sphincter is greatly multiplied.

The selection of patients for surgical correction of stress incontinence is made

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restored, provided the sphincteric muscles and nerves are intact. It is important that this test be made with a full bladder. Also the fingers should be placed on either side lateral to the midline and should merely elevate the vesical neck, not compress the urethra.

The diagnosis of true stress incontinence is further verified by cystograms made while the patient is relaxed and during voluntary straining of the abdominal musculature. The straining film demonstrates the amount of descent of the bladder neck, and this has ranged from $\frac{3}{4}$ to 2 inches (fig. 4).

If the studies indicate vesical neck ptosis to be the cause of the incontinence and if no inflammatory or neurological vesical disease is present, the patient

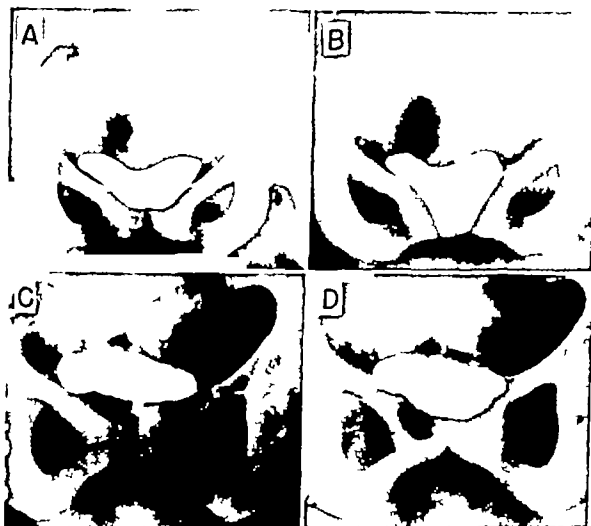


FIG. 4. Erect cystograms, patient with urinary stress incontinence. *A*, preoperative, patient relaxed; *B*, preoperative, patient straining abdominal musculature. Note descent of vesical neck. *C*, postoperative, patient relaxed; *D*, postoperative, patient straining. Actual descent of vesical neck $\frac{1}{2}$ inch.

may be assured of relief following replacement of the ptotic vesical neck to its normal position.

SURGICAL TECHNIQUE

We believe that the essential feature of a successful surgical approach to vesical neck ptosis is the construction of a support to the vesical neck area. This support must hold the bladder neck in its normal position even during periods of great abdominal stress, to be successful. Mechanically this is best done by underrunning the bladder neck with a fascial sling, using the retropubic approach. The high rate of failure of vaginal procedures designed to correct stress incontinence is undoubtedly due to the difficulty of forming a strong lasting support to the vesical neck, especially in instances where the fascia is deficient in the midline area, or where it has been destroyed by previous surgery.

The method of construction and attachment of the fascial sling is of secondary importance. Equally good results may be attained by utilizing the general technique of Goebell-Stoeckel-Frangenheim or that of Millin. The important

occurrences. Thus, the abdominal tumor is a primary finding, revealing a firm, resistant, yet painless mass. In the first case with the history of weight loss and epigastric distress, most assuredly, very near in the future, the child would have been seen by a physician and the presence of an abdominal mass found. However, it took an accidental force simulating an acute catastrophe to focus the prompt attention of the patients. Hematuria in Wilms' tumor has been reported from less than 5 per cent to as high as 20 per cent. Even here, the hematuria is always intermittent, usually with recurrences at regular intervals. As in all kidney bleeding, the blood is diffused throughout all the voided urine and in the absence of clots, is painless. Trauma, superimposed upon Wilms' tumor, may contribute to poor prognosis of the patient. At first the tumor, which is of a soft brainlike consistency with numerous areas of necrosis and cystic degeneration, is always encapsulated and localized to the area. Trauma, even though not severe may effect the rupture of the capsule and easily hasten the spread to contiguous organs. In addition, the veins of the tumor are comparatively large, yet their walls are thin and fragile and they frequently rupture spontaneously resulting in numerous infarcts. The areas of demonstrable metastasis in the lung or brain are by way of direct blood stream propagation. Trauma will materially influence the rapidity of spread through the laceration of these fragile veins. In the first case, the exact diagnosis, as to the existing pathological changes, was rather in doubt prior to the cystoscopy and pyelogram. The distortion of the upper right calyx, although not characteristic of a renal tumor, gave us our first evidence of the possibility of an existing tumor at the pole of the kidney and this helped to establish our approach to the problem, which was verified upon surgery. The second case presented a similar problem of trauma associated with previous unknown disease. Differentiation of renal injury from that of liver or spleen is quite difficult, at times, and here again one sees that when trauma has been quite mild and evidence of injury to the kidney or surrounding structure appears, it is of utmost importance to be aware of the fact that pre-existing disease of the kidney may exist. When this child was first seen, the diagnosis of a retroperitoneal trauma with hemorrhage or splenic injury was made. The child appeared to be acutely ill and an exploratory laparotomy was performed for a possible splenic injury or retroperitoneal bleeding. Upon finding a retroperitoneal tumor too large to be handled surgically, the incision was closed and a course of preliminary roentgen therapy given with subsequent surgery.

SUMMARY

Trauma to the kidney is not unusual in childhood and when evidence of renal damage is found one must always bear in mind that pre-existing disease may be present. All efforts should be made to identify the pathology of these pre-existing lesions before definitive surgery is attempted.

We have presented two cases of Wilms' tumor which have been apparently progressing in the routine asymptomatic fashion, but it took the presence of trauma to lead to their discovery. We wish to thank Dr. Sidney Rosenberg for the privilege of presenting the second case.

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When, as is common, one or more previous anterior colporrhaphies have been done, there may be rather dense adhesions between the vagina and bladder, but the dissection has not been difficult in spite of this. In the midline there is invariably a firm connection between the vagina and urethra, and this must be forcibly pierced. A long piece of heavy silk is then doubled, grasped by the forceps, and drawn through the tunnel. This suture is divided at the mid-point and each piece attached to one of the straps at the free end, after threading the strap under the lateral border of the rectus muscle (fig 5, C). Traction on the silk draws the fascial straps through the tunnel and the tension is adjusted after loosening the Millin retractor. The tension should be just sufficient to elevate the vesical neck to its normal position, and no kinking of the urethra should be observed. Usually the bladder is almost in its normal position when the patient is anesthetized and in mild Trendelenburg position, and only sufficient tension to keep it there is necessary. The straps are secured one to the other with 3 or 4 silk sutures at each side (fig 5, D). A rubber tissue drain is then laid to the space of Retzius and the fascial border approximated. There is moderate but not excessive tension on the suture line, and closure is facilitated by jack-knifing the patient. The skin is then closed and a dressing applied.

The catheter is connected to bedside bottle drainage after the patient's return to bed and is left in place about 5 days, or until the patient is able to be up without discomfort. The rubber tissue drain is removed on the third day.

When the operation is performed after the Goebel method, we have prepared one strap on each side of the midline, using rectus fascia and leaving each strap attached at the inferior end, but being careful to keep the inferior margin of the incision at least one inch superior to the pubis. From this point on the operation proceeds as outlined above, except that the straps pass through the hiatus between the rectus muscles, and of course the wound is closed vertically. This procedure can be done through a smaller incision than the Millin, and in our hands has given equally good results to date.

RESULTS AND CONCLUSIONS

Fifteen female patients have been operated on by the foregoing methods. Twelve of these patients had had from one to three previous unsuccessful vaginal operations for stress incontinence. The incontinence followed childbirth in 12 instances and occurred spontaneously after the menopause in 3. All the patients had been incontinent for at least 2 years, and two for more than 16 years. The urinary leakage in all cases was profuse and incapacitating. Preoperative cystography demonstrated the typical vesical neck ptosis during stress. The follow-up period has been from 8 weeks to 26 months, and the postoperative films have revealed normal fixation of the bladder neck during stress in every instance. The results have been excellent in 14 patients. None of these patients have experienced postoperative urinary incontinence at any time, even during periods of severe exertion. There have been no complications: no significant wound infection, no osteitis pubis, no residual urine, and no urinary infection. Failure occurred in one patient, and this was the first of the series. This patient

the suitability of this procedure, merely from inspection of the plain x-ray film, in that calculi located at a distance of 15 to 20 mm from the midline of the covec are usually accessible



FIG 1

FIG 1 Intravesical view showing cystoscopic appearance of bulge due to calculus impacted in intramural portion of left ureter

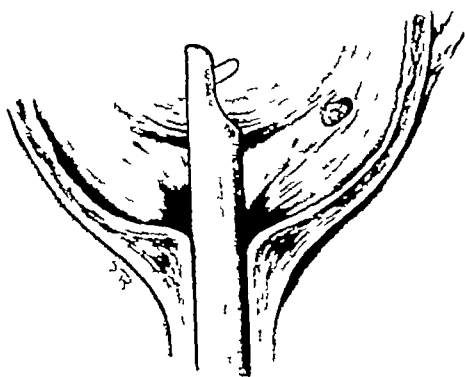


FIG 2

FIG 2 Intravesical view of calculus in intramural portion of left ureter exposed by excision of "roof" of intramural portion of ureter with resectoscope loop



FIG 3

FIG 3 Intravenous urogram of lower ureter showing impacted calculus in intramural portion of left ureter with ureteral dilatation above Case 2



FIG 4

FIG 4 Intravesical appearance of ureteral orifice and site of removal of calculus at 6 months follow up examination Not infrequently excision includes ureteral orifice

No additional equipment is necessary other than that ordinarily employed in transurethral prostatic resection. Either low spinal or caudal anesthesia is suitable. Employing the cutting current, the summit of the bulge shown in figure 1 is sliced off with the loop of the resectoscope, disclosing the calculus as shown in figure 2, after which the calculus may be dislodged by manipulation with the

BLADDER ELECTROMYOGRAPHY A NEW APPROACH TO THE DIAGNOSIS OF URINARY BLADDER DYSFUNCTION

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The conventional cystometrogram with its inherent defects has been of limited aid to the diagnosis of bladder dysfunction but has served to stimulate urologists in the study of bladder physiology. Interest thus aroused has resulted in many different types of cystometers, of which the Young investigational manometer, Rose revolving drum, Lewis constant recording card, Lowsley mechanical pressure gauge, Munro water manometer and the Simons microcystometer are examples. All of these instruments and their various modifications measure only one thing—change in intravesical pressure. They do not record bladder contractions of a magnitude less than mass movements, such as occur in an effort to void, and unfortunately they may record changes in intravesical pressure due to a diversity of extrinsic factors. Thus variation in intra-abdominal pressure, emotional instability, and many pathologic changes within the bladder (diverticula, fibrosis, ureteral reflux, tumor, etc.) frequently introduce changes in the cystometric record that are difficult of interpretation.

Recent investigators have compiled sufficient physiological evidence of the syncytial character of certain smooth muscle structures to require a careful re-evaluation of the generally accepted concepts of visceral activity. This is particularly true as regards the spread of the excitatory impulse, the intrinsic innervation of viscera, and the development of electropotential changes associated with muscular activity. Indeed, extensive studies of the bioelectric potentials in smooth muscle from the genital, gastro-intestinal and urinary systems led Bozler to conclude that certain "smooth muscle viscera may be considered physiologically as giant smooth muscle cells in the same sense as the heart may be regarded as a giant striated muscle cell." Although the bladder may not belong strictly to this category since it is so closely controlled by the central nervous system, the statement emphasizes the physiological difference between the integrated response of a smooth muscle viscus and the co-ordinated response of striated muscle bundles.

Before attempting to evaluate these concepts as they may apply to the intact human bladder, certain peculiarities of that viscus should be considered. The human bladder is unique among the viscera in the degree of its subjugation to the cerebral cortex. Not only can the bladder be activated by an effort of the will but the act of voiding which is basically a reflex activity arising in the autonomic nervous system and lower spinal cord, can be voluntarily inhibited or interrupted at any stage. Another outstanding characteristic of bladder physiology is its adaptation to a wide range of volume and internal pressure changes. The intravesical pressure during filling is primarily a reflection of the tonus of

Read at annual meeting American Urological Association, Chicago, Ill., May 22, 1951.
Note by editor: Dr. Boyce's paper was awarded a prize in the 1951 essay competition.

DISCUSSION

DR WILLIAM M COPPRIDGE (Durham, N. C.) Drs Davis, Lee and Davis have emphasized the difficulties and generally unsatisfactory results of open surgery for stones in this location. The method they describe is a valuable adjunct to treatment of these cases. Drainage of the bladder with a catheter for a period of 36 to 48 hours prevents complications that might arise from almost any type of instrumentation at the base of the bladder. Many of these patients are extremely ill, and removal of the stone by such a simple method is certainly desirable.

I should like to comment briefly on the method that was reported before this meeting in Los Angeles in 1949. The procedure consists of the passage of forceps outside the cystoscope in the female and through a perineal urethrostomy in the male. Locating the orifice, the forceps is introduced, dilating it and grasping the stone.

[Slide] This shows the forceps and cystoscope being passed alongside each other.

[Slide] Under the vision of the examining telescope, the orifice is located, and the forceps manipulated into the field.

[Slide] Here the orifice is entered, dilated, and the stone is grasped and removed.

[Slide] This slide shows a stone in the lower left ureter in a woman.

[Slide] Here the stone has been grasped and is being removed.

[Slide] This shows a somewhat larger stone in the right ureter in a male.

[Slide] The cystoscope and forceps have been introduced through a perineal urethrostomy, the stone has been grasped, and is being removed.

While we have not been able to remove all the stones we have tried by this method, we have been successful in over seventy cases.

Dr Davis and his associates have presented a valuable additional procedure to be used in this troublesome group of cases.

boundary from the depolarized to the polarized areas. Contraction of the muscle cell is therefore associated with depolarization, and recovery of the cell is associated with repolarization (fig. 1).

Injury to the muscle cell may interfere with and modify this flow of electro-potential in three basic ways: 1) There may be a change in the permeability of the membrane so that either partial or complete depolarization of the injured area results. 2) There may be inability of the injured area of the cell to respond to an adequate stimulus, or the injury may prevent the stimulus from reaching all of the muscle cell. 3) The injured cell may undergo complete or partial re-

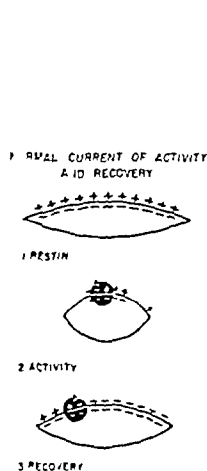


FIG. 1

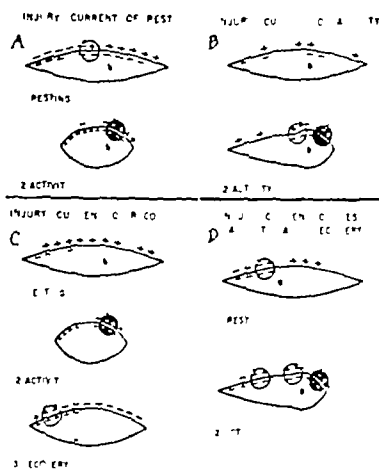


FIG. 2

FIG. 1 Electropotential changes of normal muscle cell during contraction and recovery. Activity is associated with depolarization and recovery with repolarization. Each diagram represents an individual smooth muscle cell in which changes in polarization are represented by dipoles shown along one surface of cell membrane.

FIG. 2 Electropotential changes in injured muscle cell during rest and activity. A, when injured part of cell undergoes either complete or partial depolarization but retains ability to respond to an adequate stimulus. B, when injured part is incapable of responding to stimuli but retains polarization of resting state. C, when injured part responds to stimuli but exhibits protraction of repolarization time. D, when injured part undergoes either complete or partial depolarization and also loses ability to respond to a stimulus adequate for response in uninjured part of cell.

Each diagram represents an individual smooth muscle cell in which changes in polarization are represented by dipoles shown along one surface of cell membrane. Injured area of cell is stippled, *a*, and normal area is *b*. White circle indicates current of injury. Black circle indicates normal current of activity.

polarization at a delayed rate. Injured area may therefore develop aberrant electropotential changes termed "currents of injury." By various combinations of these three basic types of injury it is possible to demonstrate that an "injury current" may occur during rest (fig. 2, A), during activity (fig. 2, B), during recovery (fig. 2, C), or during rest, activity, and recovery (fig. 2, D).

If there is a true syncretic character of smooth muscle viscera, or if the nerve net within the visceral wall effects an integral response to stimuli similar to that of a syncretium, then it should be possible to measure the electropotential developed by the mass of smooth muscle cells that compose the viscera in question. Furthermore, various degrees of injury to the viscera should be detectable by

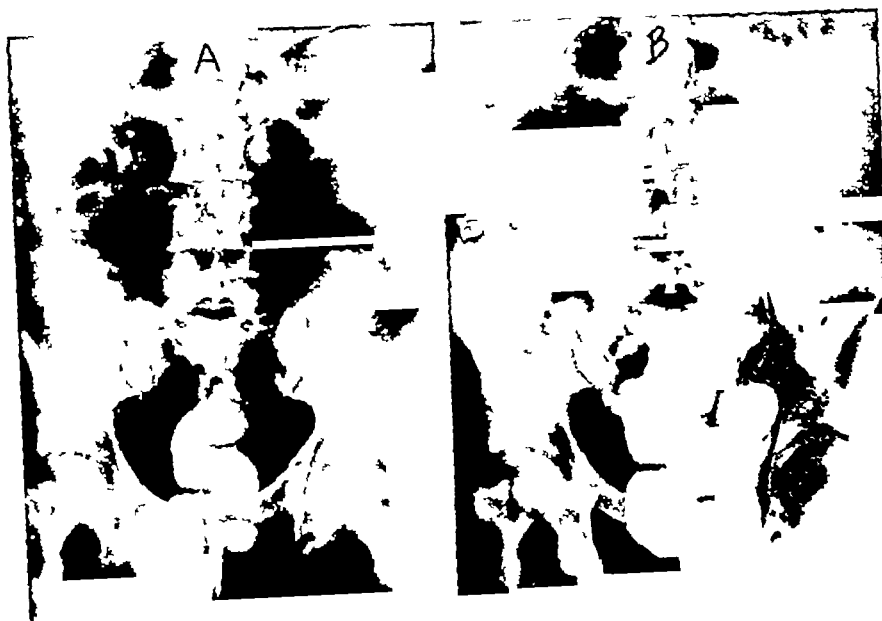


FIG 1 P E Carcinoma of bladder Cystectomy, adenectomy, and bilateral uretero-sigmoidostomy using modified Coffey 1 technique Normal voiding 200-250 cc A, 50 cc sodium iodide instilled in rectum No reflux observed B, 150 cc dye instilled in rectum demonstrating reflux



FIG 2 A, J S Carcinoma of bladder Cystectomy, adenectomy and bilateral uretero-sigmoidostomy using Nesbit mucosal technique Normal voiding 350 cc Rectogram using 200 cc sodium iodide demonstrating ureteral reflux

B, P T Carcinoma of bladder Cystectomy, adenectomy, left nephrectomy and unilateral ureterosigmoidostomy using Nesbit mucosal technique Normal voiding 100 cc Rectogram using 50 cc sodium iodide demonstrating ureteral reflux by pneumopyelogram

ureteral valve would remain competent if subjected to this persistent intrarectal pressure The normal ureterovesical valve was employed as the ideal in this phase of the experiment Dogs were used which had previously been prepared

(cystoscopy, pyelography, laboratory tests, etc.) Consultations were freely obtained from all other departments in the hospital in an effort to evaluate each patient completely and to establish an accurate diagnosis of any pathologic conditions other than intrinsic urinary tract disease. Data were kept on each patient

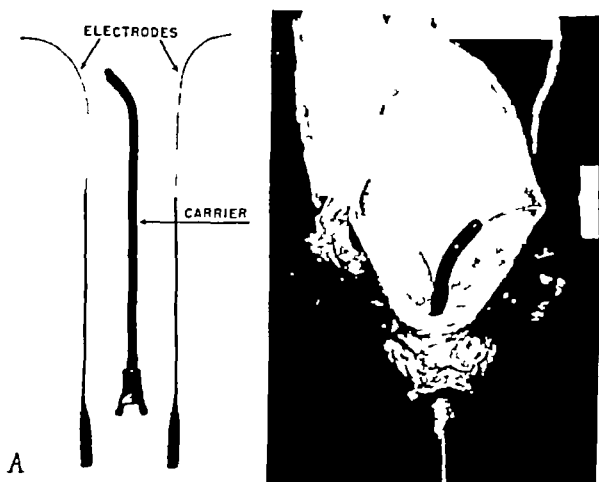


FIG. 3. A, bladder electrodes and plastic electrode carrier which contains insulated channel for each electrode. B, autopsy specimen of normal bladder and prostate. Anterior portion of bladder removed to demonstrate position of electrodes during electromyographic examination of bladder.

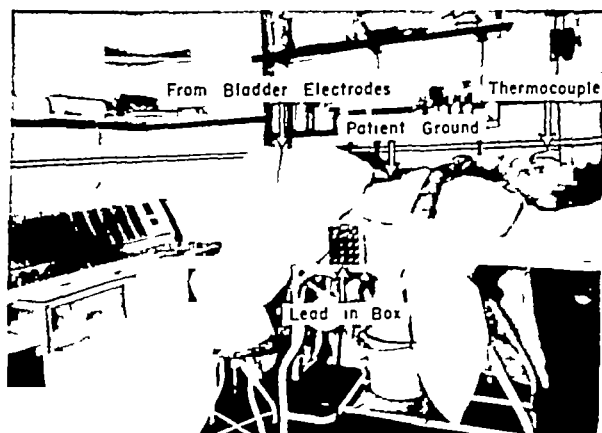


FIG. 4. Position of patient during electromyographic examination of bladder. Patient placed on ordinary examining table with stirrups. Electrode carrier is introduced into bladder and after electrodes are brought into contact with each lateral bladder wall instrument is held in position by bridge of adhesive tape between stirrups of the examining table. Lead in box from electroencephalograph attached to side of table where it is readily accessible to three leads from patient, namely, leads from bladder, patient ground, and thermocouple. Electroencephalograph is Grass instrument model III C.

in a file, which included history, physical examination, laboratory studies, and notes on follow-up visits to the hospital. Repeated examinations by the electromyographic method were made from time to time, particularly when there was indication of change in the course of the urinary tract disease or of bladder function.

bladder Round cell infiltration was also noted frequently Ureteral and vesical epithelium was many times thickened (fig 4) Occasionally bladder epithelium assumed a glandular pattern resembling that found in small bowel This finding was not observed in the ureter

In three dogs at the time of autopsy urine was taken for culture from the rectum and each renal pelvis Although the organisms recovered were not the same for all animals it is significant that for each dog the bacteria were identical in the three locations sampled

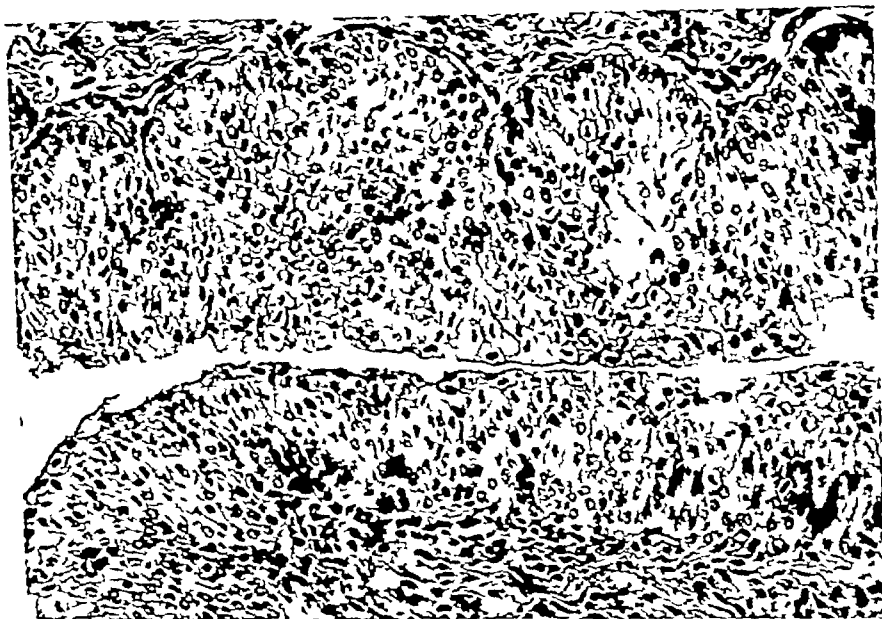


FIG 4 Dog 296 Vesicorectal anastomosis Sixteen months postoperative Photomicrograph of ureterovesical junction Bladder on left Epithelial proliferation, peri-ureteral fibrosis and incompetency of valve demonstrated

DISCUSSION

Following uretero-intestinal implantation certain patients will have fibrosis and stricture formation at the site of the anastomosis with resulting renal damage Himmán and Weyrauch have demonstrated that during the reparative stage local infection contributes greatly to the peri-ureteral fibrosis It is not surprising that another group of patients having a well-constructed anastomosis with minimal fibrous tissue reaction will perforce have ureterorenal reflux of fecal contaminated urine The prime function of an anastomosis is patency of the stoma to provide adequate urinary drainage Regurgitation is therefore potentially possible Mathis has reported spontaneous pneumopyelograms following uretero-intestinal anastomosis Recent procedures devised to reduce stricture formation by direct mucosal anastomosis would appear to foster reflux Whisenand and Moore have observed feces draining from nephrostomy tubes in such a patient Similar experiences by others have been reported In these cases dilatation of the upper tract develops with pyelonephritis and impaired renal function

trace. Irregularities, or rapid sharp deflections of the recording needle during the trace, are reflections of muscular change and indicate interference with either development or conduction of the electropotential through the muscle mass. This may be due to areas of altered conduction, to inactive or "silent" areas (fibrosis or separation of muscle fibers), or to modification of the major electropotential by localized injury currents which may either augment or reduce (cancel) the major electropotential.

3) Electromotive force (emf) (fig. 5). The electropotential developed in each phase of the wave and recorded in millivolts by measuring the maximum excursion of the oscillograph and calculating from the calibration figure of the particular setting of the machine.

4) Time (fig. 5). The duration in seconds occupied by each phase of the wave and measured from the point at which the recording pen leaves the base line to the point at which it returns. This is easily calculated from the time calibrations on the recording tape.

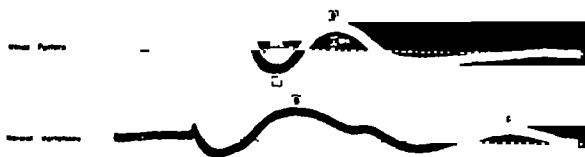


FIG. 5. Diagrammatic enlargements of actual records to demonstrate methods of measuring time and electropotential difference and to illustrate variations encountered in normal bladders.

Superior trace is an enlargement of a single normal wave. Time (sec.) is measured along base line (dotted line) and electropotential difference (Mv.) is measured at right angles to base line. Inferior trace is composite enlargement of several records to demonstrate all variations encountered in normal.

5) Voluntary control (fig. 6, C). Ability of the patient to produce a voluntary contraction of the bladder with characteristic wave formation as shown by the record.

1. *The normal bladder.* Twenty patients were considered to have a normal urinary system and the following data have been derived from a summary of observations made on this group.

The normal bladder evidenced rhythmic smooth muscle contractions by characteristic wave-like deflections of the recording oscillograph. These waves occurred at an average frequency of 2.4 waves per minute and with a constant rhythm. The waves were di-phasic with deflection of the needle in opposite directions from the base line in each phase. By way of standardization, the polarity of the electrodes was arbitrarily set so that the initial phase was a deflection below the base line and the second phase was above the base line. The first deflection of the oscillograph was termed the A phase and the second deflection the B phase (fig. 6, 1). The average duration of potential change in the entire wave (A and B components) was 4.73 seconds. The A phase showed a duration of 1.35 seconds and the B phase an average duration of 3.38 seconds. The average peak electromotive force was 0.283 millivolts for the A phase and 0.366 millivolts for the B phase.

This reflux usually occurs before the desire to "void"

Direct mucosa-to-mucosa anastomosis of ureter to bowel tends to reduce stricture formation at the stoma but encourages regurgitation

Should a technique be developed for the construction of an ideal uretero-intestinal valve experimental evidence is presented that it would subsequently become incompetent due to increased intracolonic pressure. Of the dogs so studied 100 per cent developed renal disease and 60 per cent died within 19 months

The advisability of higher ureteral implantation and the necessity of more frequent "voidings" have been discussed

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curled in about 10 per cent of individuals, both normal and abnormal, but was constantly present in the particular record in which it did occur. Normal variations in the B phase were much more common, as evidenced by minor deflections or "wavers" of the oscillograph. These "b" phases occurred 1 to 3 times in the normal B phase when present, but were seen in only one fourth of the normal group (fig 6, *B*). These variations of "wavers" rarely occurred in the C phase of spontaneous origin but were the rule in C phases of voluntary contraction when the patient "strained" to void.

Differentiation between the electromotive force developed from the bladder itself and that emanating entirely from other surrounding muscle proved to be no problem, since the latter was absent except in the rare paraplegic patient with spasm of the extremities. The deflections of the oscillograph due to such massive muscular movements were readily identified after even brief experience with the technique described.

In the occasional patient, however, slight rhythmic deflections from the base line appeared which were obviously coincidental with respiratory changes in intra-abdominal pressure. The respiratory origin of these deflections was verified by observing simultaneous recordings from the bimetallic thermocouple which was always placed beneath the patient's nares. The electropotentials developed from the changes in temperature with inspiration and expiration were amplified and recorded on the record simultaneously with the bladder electropotentials. Thus artefacts due to respiratory activity were readily identified and offered no difficulty in the interpretation of the electromyographic record.

The relationship of these electropotential changes to change in intravesical pressure was studied by means of a simple water manometer attached to the central drainage tube of the electrode carrier. Coincident with the spontaneous A phase there was no demonstrable increase in the water level of the manometer, on the contrary, with voluntary effort to void there was a coincident decrease in the intravesical pressure. A definite rise in intravesical pressure occurred simultaneously with the development of the B phase and subsided as the B phase regressed. This change in intravesical pressure was very much greater in B phases which occurred during voluntary efforts to void than in those associated with spontaneous contraction. When the C phase was present (as universally occurred during voluntary attempts at micturition), there was a coincident and prolonged elevation of the water in the manometer, suggestive of a sustained tonic contraction of the bladder musculature.

B The abnormal bladder. Certain changes in the electropotential record appeared to be characteristic for the following changes in either the bladder musculature or its innervation.

I. Muscular hypertrophy (fig 7, table 1). This group consisted of 18 patients with early hyperplasia of the prostate or urethral stricture. Each of these patients was demonstrated to have trabeculation of the bladder without cellul formation and with less than 30 cc. of residual urine.

a) Rhythm was regular

by extensive urological study, including cysto-urethroscopy, upper urinary tract visualization, and cystometry. Neurological causes for vesical dysfunction are eliminated and intrinsic vesical and urethral disease ruled out. The patient

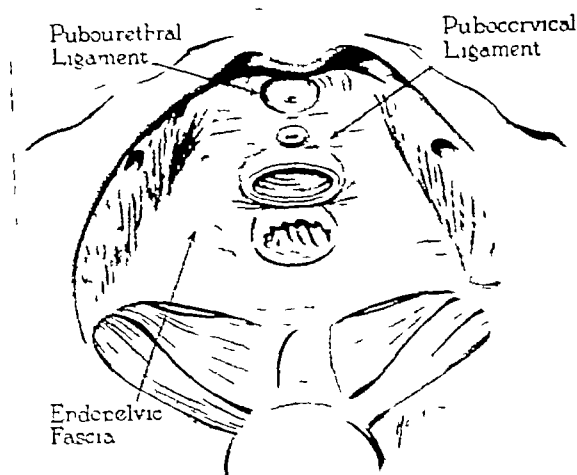


FIG 1 Female pelvic diaphragm and its fascial covering viewed from above. Fascia attached at pubis and arcus tendineus forming hammock-like support to vesical neck.

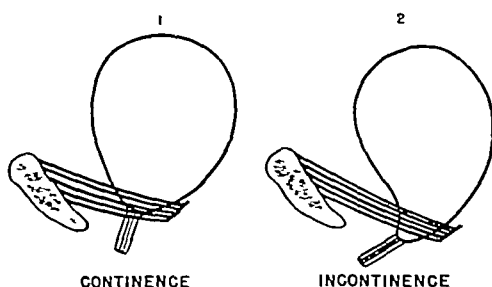


FIG 2 Diagrammatic representation of position of vesical neck when fascia is torn or weakened.

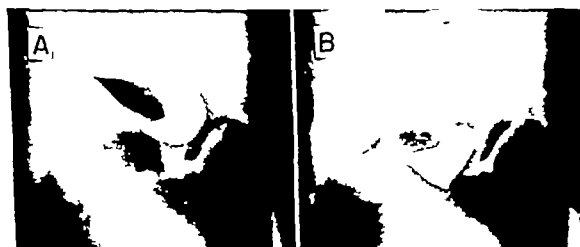


FIG 3 Oblique cystogram, urinary stress incontinence. A, patient relaxed; B, patient straining abdominal musculature.

is then tested for continence by having her cough vigorously after the bladder has been filled to capacity with sterile water. If leakage occurs, the bladder is refilled and two fingers are introduced into the vagina, replacing the vesical neck to its normal position by manual vaginal pressure. Continence is then

present and were proportionate to the degree of observed pathologic change noted on cystoscopy. These changes from the normal were evident in all phases of the electromyogram.

c) Electromotive force was diminished throughout, more particularly in the B and C phases.

TABLE 1 *Comparison of electropotential changes in the normal and abnormal bladder*

	RHYTHM	WAVE FORM	ELECTROMOTIVE FORCE	TIME OR DURATION	RESPONSE WITH VOLUNTARY EFFORT
Normal bladder	Regular 2-4 per minute	Constantly smooth and uniform	A 0.283 mv B 0.366 mv C 0.290 mv	A 1.35 sec B 3.38 sec C 3.54 sec	Prompt response C wave constantly present
Muscular hypertrophy	Regular 1-2 per minute	Smooth and uniform	Increased and uniform	Normal or slightly increased	Prompt response C wave constantly present
Muscular degeneration	Irregular Quiescent intervals of 1 to 3 minutes	Irregular and variable	Decreased but uniform	Decreased	Delayed response C wave variable but present
Hypoactive "shocked" neurogenic bladder	Absent or long intervals of quiescence 10 to 20 minutes or more	Smooth and uniform	Decreased but may approach normal Variable	Decreased but may approach normal	Absent
Hyperactive "spastic" neurogenic bladder	Alternate rhythmic activity and quiescence	Smooth Quite variable in spasm	Variable Marked increase (3 to 8 mv) alternately very low (0.1-0.2 mv)	Quite variable Frequently decreased	Absent or initiated with difficulty Form is variable

d) The duration of the entire wave complex was found to be decreased, shortening being relatively greater in the B and C phases. Note that in these cases time was usually in direct proportion to the electromotive force developed, in contrast to the neurogenic bladder where this relationship may be reversed (Compare figs. 8, B and 9, B).

e) Voluntary effort to void usually resulted in a prompt electropotential response, but in some instances repeated attempts were necessary to initiate the

feature is the construction of a securely attached, sufficiently wide sling which elevates the bladder neck permanently into its normal position. It is not likely that any of these slings act as a movable "puckering-string" as has formerly been the conception. The end result can be demonstrated to be merely a scarred, fixed support, substituting for the natural hammock of the pubo-vesico-cervical fascia.

The operation, performed by Milin's method, is as follows. The bladder is emptied by an 18F, 5 cc Foley catheter which is used for postoperative drainage.

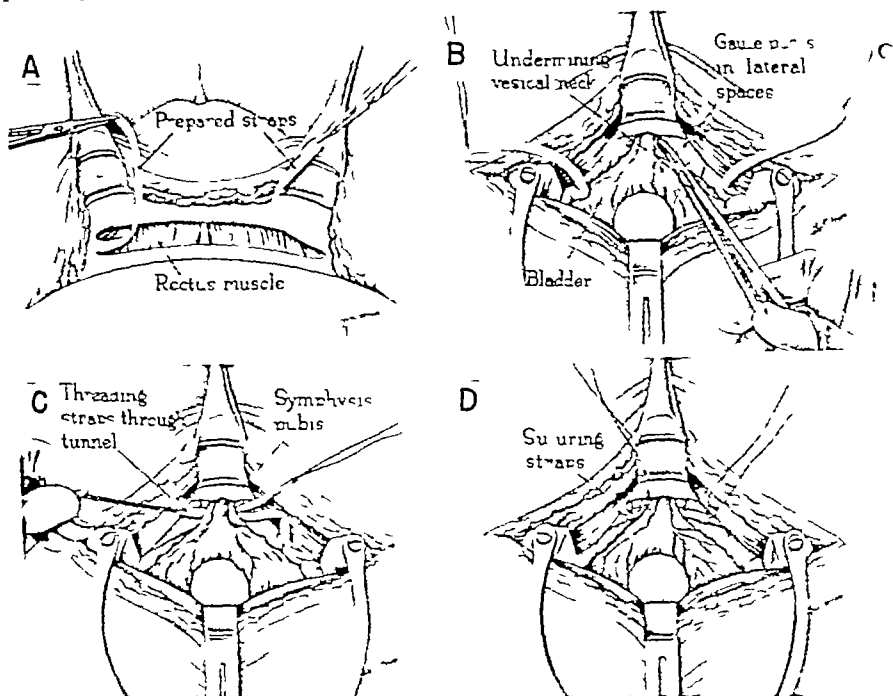


FIG 5 Operative technique (after Milin). A, transverse suprapubic incision in skin and anterior fascia. Two straps are prepared 1 cm. wide. B, tunnel prepared beneath vesical neck. Straps are threaded lateral to rectus muscles. C, straps threaded through tunnel. D, sponges removed and straps sutured to each other under sufficient tension to replace vesical neck in normal position.

After preparation, a 5 inch transverse incision is made 1 inch above the superior edge of the pubis, and is carried down to the external aponeurosis. Two straps are then fashioned from the rectus and external oblique aponeurosis, being left attached at their lateral aspects (fig 5, A). It is important to have these straps at least 1 cm. wide. The rectus muscles are then separated in the midline and the retropubic space entered. The urethral catheter is palpated and the vesical neck area identified by the catheter bag. A Milin retractor is inserted and by careful sponge dissection the lateral fossae of the urethral area opened. At this point the urethra with its milking catheter is grasped by a long Babcock forceps. The urethra is underrun at its junction with the bladder, using a Mixer clamp or an aneurysm needle (fig 5, B).

a reversal of polarity in an occasional wave complex, either of spontaneous or voluntary origin, that is, the A phase become an upward deflection, while the B phase was represented by a downward movement of the recording stylus (fig 8, A)

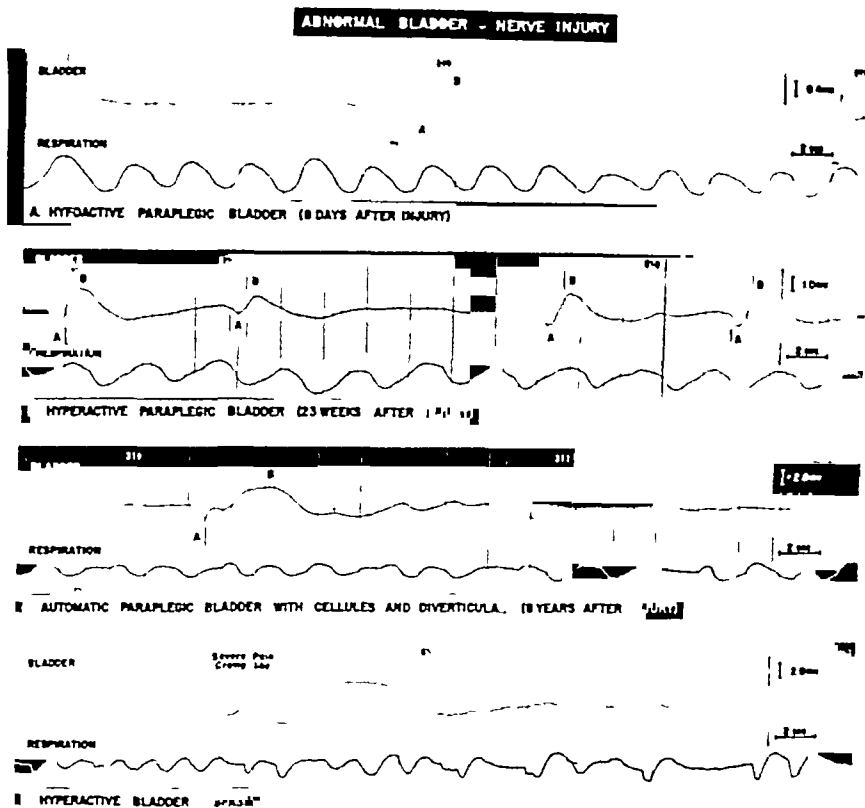


FIG 9 Examples of electromyographic records from bladders of patients with spinal cord injury

A, hypoactive paraspastic bladder 8 days after gunshot wound of second lumbar segment of spinal cord. This is only wave present in 15 minutes of observation. Note similarity to normal bladder wave in figure 6, 1.

B, hyperactive paraspastic bladder 23 weeks after fracture of seventh cervical vertebra. This patient passed urine in small quantities almost continuously.

C, spontaneous wave in patient with injury of twelfth thoracic vertebra of 8 years' duration. There were a few cellules and one diverticulum of bladder. Note distortion of B phase and compare with figure 8.

D, typical bladder spasm with pain occurring spontaneously during electromyographic examination of bladder. Note abrupt changes in trace indicating rapid excursions of needle with plateau shape of peak phases which indicate electromotive force greater than capacity of oscillograph.

III The neurogenic bladder (fig 9 table I). All of this group of 25 patients had suffered injury to the spinal cord.

A. The hypoactive bladder. Eight patients were observed immediately after injury when the history, physical examination, and the conventional cystometrogram indicated a hypoactive or "shock-type" bladder.

was a 47 year old housewife, who had become incontinent 15 years previously, following childbirth. She had had 3 previous vaginal operations of the Kelly plication type for her stress incontinence, and all had failed. There was only 1 cm. of urethra left and the anterior vaginal wall was extensively scarred. A Millin operation was done with a perfect result, complete continence being restored. On the fortieth day following surgery she lifted a heavy coal scuttle and stated "she felt something break in the abdomen." This was immediately followed by a leakage of urine and her stress incontinence has been present ever since. It was apparent from pelvic examination that the sling had broken and the bladder neck ptosis recurred, this was confirmed by cystography. In retrospect it was remembered that the straps had been prepared only one quarter of an inch wide, and we believe this to be the cause of breakage. This patient demonstrated most vividly that a normally placed bladder is essential for normal sphincteric activity. When the support was disrupted her initial urinary stress incontinence was immediately re-established and has continued to date.

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change but to produce wave forms which were essentially normal in character when voluntary efforts to void were induced. On the other hand, some patients with involutional melancholia and acute depressed states exhibited a normal or even slightly increased spontaneous electropotential activity. Such persons tended to be uncooperative or else to experience much difficulty in initiating voluntary efforts to void.

DISCUSSION

Comparison of the results in these 105 patients suggests that the electropotential changes observed are of muscular origin, and that the oscillographic trace represents the vector sum of all of the excited individual muscle cells of the bladder. The muscular activity is, of course, initiated by a spreading of the excitatory impulse, and this may coincide with the initial A phase. This premise is based on the following correlations between the electropotential changes and muscular activity:

1) The A phase is considered to represent the spread of the excitatory process through the muscle mass since it is an initial phenomenon unassociated with coincidental muscular contraction but always followed by contraction. The precursory spike potential, or "a" phase, is only occasionally present and is possibly a reflection of the nerve impulse or of some unknown "trigger mechanism." Appearance of this spike potential ("a" phase) in certain records and its absence in others may be due to the chance placement of one electrode near the "pacemaker" or site of origin of the nerve impulse in the detrusor muscle. Evidence that the A phase is unassociated with muscular contraction is based on observations of coincidental changes in a water manometer. The lag in such a mechanical system is, of course, quite long when compared with an oscillographic recording of electropotential changes and raises the possibility that such lag may account for the absence of a detectable change in the manometer. The initial A phase is developed on the oscillograph. On the other hand, the close correlation between changes in the manometer and the B and C phases strongly suggests that these components accompany bladder contraction.

The small diminution in intravesical pressure associated with the A phase in voluntary efforts to void is considered to be coincidental, since it was not noted during spontaneous bladder activity. This slight diminution in intravesical pressure just prior to voluntary effort to void has been noted by Denny-Brown, who attributed it to a fall in intra-abdominal pressure induced by relaxation of the perineum. It is not possible in these experiments to exclude the possibility that a diminution in tonus may immediately precede every contraction of the bladder musculature. If such were the case, it would account for both the electropotential change and the decrease in intravesical pressure as well. Such seems unlikely in view of the fact that electropotential changes have not been demonstrated to accompany tonus changes in smooth muscle.

That the A phase reflects the spread of the excitatory process seems the more likely explanation for its occurrence in view of the fact that an initial potential change as a precursor to muscular contraction is an almost constant finding in cardiac, skeletal and smooth muscle. Moreover, most investigators have considered this initial electropotential to be synonymous with the excitation process.

the detrusor muscle, and this pressure remains amazingly low and constant during normal filling. In the process of filling from 0 to 500 cc the intravesical pressure remains relatively constant, below 12 to 18 cm of water. Pressure during emptying is due to the contraction of the detrusor and trigonal musculature and may rise to 130 cm of water.

Both the tonus and contractile mechanism of smooth muscle play an important part in bladder physiology; however, these two characteristics of smooth muscle have little in common. Contraction of the smooth muscle cell is a shortening of its long axis that follows an adequate stimulus, while tonus may be defined as the resistance which the substance of the cell offers to stretching. The rhythmic contractions exhibited by all smooth muscle viscera are superimposed on the tonus state, and the two may vary independently of each other. By way of further differentiation, the stimulation of tonus nerve fibers in the bladder is mediated by the production of acetylcholine, but this is not true of stimulation of the contractile nerves. Furthermore, the contractile mechanism is characterized by fatigability, expenditure of energy, heat production and the development of an electromotive force. The tonus mechanism is relatively insusceptible to fatigue and is maintained with a negligible expenditure of energy without measurable heat production or development of an electromotive force.

It is clearly apparent that any method of evaluating the functional capabilities of the intact human bladder must take into consideration a multiplicity of factors: a) neural function including cerebro-cortical control; b) tonus of the detrusor muscle; and c) contractility of the detrusor and trigonum. The following report is concerned primarily with the contractile mechanism of the bladder as recorded by the electropotential changes developed during muscular contraction. However, control by the cerebral cortex and the effect of the tonus mechanism have been kept constantly in mind and evaluated by the procedures to be described.

HISTORICAL BACKGROUND AND THEORY OF ELECTROMYOGRAPHY

The development of an electromotive force about an active muscle has been recognized since 1856 when Köelliker and Müller demonstrated the currents about the beating animal heart. Experiments published by du Bois-Reymond in 1860 demonstrated that electric currents generated in wounded animal tissues differ from those produced by normal tissues. By 1890, Ostwald had suggested a mode of origin and development for these electropotentials which has subsequently been formulated into the generally accepted "membrane theory." This theory predicates that the electrolytes within a muscle cell differ from those of the extracellular fluid both in kind and in individual concentration. These different intracellular and extracellular electrolyte solutions are separated by the semi-permeable cell membrane, and ions become aligned along the two surfaces of the membrane—positive ions on the extracellular and negative ions on the intracellular side, so that the cell membrane may be said to be "polarized" in the quiescent state. An adequate stimulus applied to the cell results in a change in membrane permeability, so that a shift of electrons occurs across the membrane and a current develops. This current flows rapidly along the cell

the oscillograph (fig 9) If these electropotentials were of neurogenic origin, the converse relationship would be anticipated

8) The absence of a detectable "repolarization" potential in these experiments is not of necessity contradictory to the concept that the recorded potential changes are of muscular origin The amplification setting of the instrument, which was maintained at a sufficiently low level to keep the A and B phases within the range of the instrument, might well have been too low to record the smaller electropotentials of repolarization Note that repolarization progresses along the muscle cell more slowly than does depolarization and so requires a longer time interval for completion Also the magnitude of change in the electrical field is less at any given instant than in the comparable stage of depolarization, although in normal muscle the area enclosed by the oscillographic deflection due to depolarization should equal that due to repolarization

Failure to demonstrate a repolarization "wave" in these experiments might also be related to rearrangement of the transverse and circular layers of muscle cells during contraction, since parallel muscle cells reinforce each other in the production of an electric field, whereas potentials from cells whose long axes are at right angles tend to cancel each other

The diagrams presented in figs 1 and 2 are greatly simplified illustrations of a most complex biological phenomenon and so are subject to just criticism if analyzed in detail This simplicity may be justifiable in that the diagrams embrace the basic concepts of the membrane theory and furnish a point of reference for discussion Cell "boundary" is much more descriptive of the living cell than "membrane", since the former carries the connotation of a living part of the cellular protoplasm, which it must be in order to explain selective interchange of ions and other dynamic activities The cell "membrane" in the sense of an inert cellophane-like casing for cellular protoplasm exists only in fixed pathologic specimens There is much evidence that during activity the membrane becomes polarized in the opposite sense rather than merely depolarized Use of the term "current" may be challenged in that it carries the connotation of a flow of electrons along a conductor, whereas the bioelectric potentials recorded in these experiments are changes in an electric field as measured by the difference in potential between the two electrodes Furthermore, these changes in the electric field may be due to molecular reorientation as each dipole is successively reversed in the activated membrane The correlation of these bioelectric potentials with other cellular functions remains unknown especially the relation to conduction of the nerve impulse, the humoral mechanism (acetylcholine, thiamin, and sympathin) and metabolic activity is influenced by inorganic and organic ions particularly those with polar structure Some investigators believe the initial potential is simultaneous with production of sympathin while the delayed potential is a function of muscular contraction and that these two may vary independently Note that disparity between the electromotive force developed and the mechanogram of isolated smooth muscle has been frequently reported as well as variation in the electric response of muscle under influence of estrogenic hormones curare epinephrin and various toxic substances The diversity of the electromyograms described by various investigators may be ascribed to a number

modification of the electropotential developed by the injured viscus. Qualitative and quantitative recording of this electromotive force to evaluate the function of the muscle producing it has been accomplished by clinicians since Einthoven made his electrocardiograph machine. Development of the electron tube with present-day methods of amplification permitted Berger in 1929 to record the electropotentials from the head and so to introduce electroencephalography. It therefore appeared probable that action potentials originating within the smooth muscle of the bladder could be recorded with modern electronic equipment, but during even preliminary consideration several problems became immediately apparent:

- 1) The electrodes should be of a nonpolarizing substance which can be closely applied to the bladder musculature.

- 2) A standard point of contact with the bladder musculature should be selected to include a constant amount of muscle tissue between the electrodes, and electrode placement should be capable of accurate reduplication in the same patient and in different patients.

- 3) Since activity of the bladder varies with the degree of filling, some standard of bladder distention should be selected and duplicated in each experiment.

- 4) It must be possible to distinguish the electromotive force developed in the bladder from that generated in neighboring muscle masses, that is, skeletal muscle, bowel, uterus, and other viscera.

MATERIALS

The electrode carrier* was constructed in the form of a plastic sheath, the central cavity being an open tube for emptying or filling the bladder. Two lateral compartments house retractable electrodes of silver-silver chloride or non-magnetic steel alloy. The Shedlovsky silver-silver chloride electrode is probably the most satisfactory. The handles of the electrodes contain connections for attachment to the lead-in box of a standard Grass electroencephalograph (fig. 3).

A bi-metallic thermocouple was constructed for placement before the nares of the patient and connected to the lead-in box of the electroencephalograph (fig. 4). This arrangement permitted simultaneous recording of respirations and ready identification of any deflection of the bladder trace due to respiratory activity (artefact).

An indifferent electrode, or patient ground, was uniformly applied exactly in the midline of the abdomen just above the umbilicus, and attached to the lead-in box. This was a small-surface electrode of the standard electroencephalographic type, held in place by electrode paste and a few strips of adhesive tape (fig. 4).

Over 100 patients have been studied by this method to date, with 1 to 5 electromyograms having been secured from each individual. The subjects were carefully chosen from either the out-patient or in-patient population of the University of Virginia Hospital and were selected for study only after thorough evaluation by all of the usual diagnostic procedures available to the urologist.

* The American Cystoscope Makers, Inc. have generously contributed the several electrodes used in these experiments.

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METHOD OF ELECTROMYOGRAPHIC EXAMINATION OF THE BLADDER

The patient was asked to void and completely empty the bladder before being placed on the examining table. The plastic electrode carrier was then introduced into the bladder and any residual urine collected through the drainage tube contained in the shaft of the instrument. The bladder capacity was determined by attaching an irrigating set to the drainage tube and filling the bladder. The electrodes were then extended from the carrier so that the contact points lay as far apart as possible, the carrier was gently withdrawn until the electrodes engaged on each lateral bladder wall (fig. 3), and then the bladder was completely emptied and the drainage tube left open in order to assure an empty bladder during the remainder of the procedure. The instrument was stabilized in this position by a bridge of tape between the stirrups of the examining table. Thus a measured and constant amount of electrode surface was exposed to a segment of bladder which was relatively constant in both size and anatomical position. The leads from the electroencephalograph were then connected to the handles of the electrodes, the thermocouple placed before the nares, and after the ground electrode was taped to the abdomen, all preparations for electromyography of the bladder were complete.

The oscillograph was run at its slowest speed (15 mm. of tape per second) and the respirations recorded on one channel of the instrument while the bladder potential changes were synchronously recorded on the adjacent channel. For the normal bladder the 9-9 setting at $\times 1$ amplification on the EKG circuit usually gave waves of such amplitude as to remain just within the limits of the recording mechanism, but amplification could readily be changed for any individual patient in order to keep waves of greater or lesser electromotive force within the range of the oscillograph. The record was discontinued after the observer was satisfied that several minutes of continuous recording had given a full and representative range of the rhythm, electromotive force, and configuration of the waves characteristic of the bladder activity of the subject. Amplification was then reduced slightly (6-9 setting at $\times 1$ amplification) and the patient was asked to void. After this attempt had been repeated to the observer's satisfaction, the machine was calibrated at all amplification settings used during the examination. This was the final step in the examination and permitted measurement of the electromotive force developed in any wave recorded during the test, the entire time required for an average examination being from 15 to 20 minutes.

Complete comfort and cooperation on the part of the patient was found to be essential for a successful result. A quiet examining room, gentle manipulation of the bladder electrodes and reassurance of the patient usually resulted in a satisfactory record.

RESULTS

The principal factors to be observed in interpretation of the bladder electromyogram are

- 1) Rhythm. The regularity of occurrence of the spontaneous waves and the "rate" or number of waves per minute.
- 2) Wave form (fig. 5). Smooth or irregular configuration of the oscillographic

superimposed upon the record and so were easily recognized and were more of an aggravation than any real interference

Rhythmic electropotential changes of short duration have been encountered on rare occasions which were in exact rhythm with the pulse rate and which we believe to have been due to pulsations in one of the adjacent great arteries. These were promptly eliminated from the record by re-setting the electrodes

Movements of striated muscle must be over a wide range, such as full extension of the knee joint or the spasm that may occur in the paraplegic patient, before any aberrant electropotential difference is recorded through the bladder electrodes. These excursions of the oscillograph are so sharp in appearance and of such great magnitude as to be impossible to confuse with electropotential changes from the bladder

Average values for electromyographic records from the normal bladder

SEX	WAVES PER MINUTE	DURATION IN SECONDS		POTENTIAL DIFFERENCE IN MILLIVOLTS	
		A Wave	B Wave	A Wave	B Wave
F	2 2	1 30	3 72	0 293	0 322
M	2 1	1 12	3 08	0 258	0 345
F	3 1	1 58	3 91	0 219	0 340
M	2 0	1 65	3 13	0 271	0 359
F	2 2	1 23	3 30	0 283	0 445
M	2 1	1 61	3 42	0 192	0 340
F	2 6	1 26	3 13	0 272	0 366
M	2 2	1 33	3 19	0 232	0 341
F	2 2	1 42	3 21	0 228	0 352
M	2 5	1 14	3 30	0 276	0 358
I	2 3	1 32	3 21	0 280	0 363
I	2 1	1 55	3 40	0 277	0 318
Av	2 3	1 37	3 33	0 265	0 357

Movements of the bladder wall, either contractions instigated by sudden changes in intra-abdominal pressure (coughing) or passive movement brought about by changes in intra-abdominal pressure, are largely eliminated from the record by keeping the bladder empty. When present, they are promptly identified by comparison with the adjacent respiratory record which is derived from the nasal thermocouple. Such artefacts intentionally produced by manual kneading of the abdomen or by sliding the electrodes about in the bladder always produced *monophasic* waves which were quite different from those of normal bladder activity.

Artefacts due to interference from 60 cycle current, mechanical disturbances within the machine or electrode circuits are readily apparent from the irregular and sharp excursions of the oscillographic needle. These annoyances are of course corrected by the proper mechanical adjustment.

In summary, electropotential differences are so universally present in living tissues and in any electronic apparatus as to present an ever present threat of

Following the spontaneous A and B phases there was an occasional prolonged elevation of the base line which has been labeled the C phase. In the spontaneous activity of the empty bladder this was only occasionally present, but with voluntary efforts to void this C phase was a most characteristic component of the trace, being universally present in the normal bladder. The duration of the

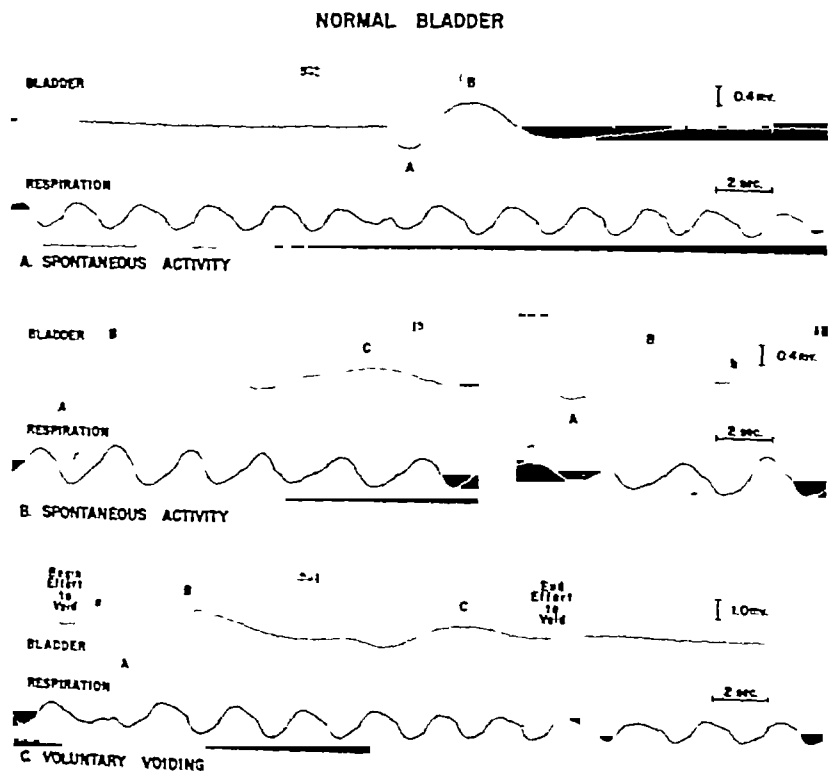


FIG. 6. Examples of electromyographic records from patients with normal bladders. Bladder trace is superior line and respiratory trace is inferior line in each record. Electropotential change is indicated by vertical millivolt (mv) scale in upper right corner and time is indicated by horizontal scale (seconds) in the lower right corner of each record.

A typical diphasic wave showing downward A and upward B phases. This is usual spontaneous activity recorded from normal bladder with regular rhythm and rate of 2-4 waves per minute.

B variations of wave form which are only occasionally present but are considered to be within range of normal. Note a C phase in first record and little "b" phase in second record. (These two illustrations are from different patients.)

C result of voluntary effort to void. Note initial little "a" phase and change in respiration at point of "begin effort to void." Also note that excursion of oscillograph needle equivalent to 1.0 millivolt in C is equivalent to 0.4 millivolt in A and B.

C phase averaged 3.54 seconds with an average peak electromotive force of 0.290 millivolts. In voluntary efforts to void the C phase developed an average peak electromotive force of 0.342 millivolts with an average duration of 4.22 seconds.

The only variation observed in the A phase was a sharp initial deflection above the base line which occurred in certain individuals (fig. 6, C). This was of very short duration (less than 0.3 second) and has been labeled the "a" phase. It oc-

CARCINOMA OF THE BLADDER INFLUENCE OF DEPTH OF INFILTRATION ON THE 5-YEAR RESULTS FOLLOWING COMPLETE EXTIRPATION OF THE PRIMARY GROWTH

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When carcinoma already has spread beyond the bladder, either by local extension or metastasis, simple extirpation of the entire primary growth in the bladder wall obviously will not rid the patient of his disease. The results, therefore, 5 years or more after total extirpation of the local growth should indicate fairly accurately which tumors at the time of operation had been completely confined to the bladder wall, and which already had spread beyond it.

The following series of 80 cases of infiltrating carcinoma consists of 39 treated by simple cystectomy and 41, by segmental resection in which the whole thickness of the bladder wall was removed with an adequate margin around the tumor it contained. These patients were operated on prior to February 1, 1946, and survived operation. The figures indicate that the 5-year survival rate is reasonably high in the group of tumors infiltrating less than halfway through the muscularis, and very low in the group showing deep infiltration.

Four degrees of infiltration were recognized (fig 1). These were submucosal, superficial muscular (less than halfway through), deep muscular (halfway through or more), and perivesical. For practical purposes, however, it was convenient to consider the first two as one group of superficially infiltrating tumors, and the last two, as a separate group of deeply infiltrating tumors. These groups were accurately determined by microscopic sections taken through the whole thickness of the bladder wall at the site of deepest infiltration.

Fourteen of 19 patients with superficially infiltrating tumors (74 per cent) lived 5 years or longer without evidence of cancer, whereas only 2 of 61 patients with deeply invading tumors (3 per cent) survived 5 years (table 1). On the other hand, only 10 per cent of the patients with superficially infiltrating tumors died with pelvic recurrences or metastases, as compared with 85 per cent of the patients with deep tumors.

The histologic pattern of the tumors in the group of patients living 5 years or longer without cancer was similar to that in the group dying or living with malignant disease (table 2). The only 2 differences were the predominance of epidermoid carcinoma, and the presence of 2 cases of adenocarcinoma and 3 of mucus cell carcinoma in the considerably larger group of deeply infiltrating tumors.

Slightly differentiated and undifferentiated tumors are admittedly the most malignant. These occurred in 37 per cent of the patients who lived 5 years or longer without cancer, and in 54 per cent of the patients who eventually died or are still living with cancer—a difference of only 17 per cent in the 2 groups (table 3).

The patients subjected to segmental resection fared a little better than those

Read at annual meeting American Urological Association, Chicago, Ill., May 22, 1951.

- b) Wave form was normal
- c) Electromotive force exhibited general increase in all phases, more marked in the B and C deflections (fig 7, A)
- d) Time factor was normal or slightly increased throughout, particularly in the B and C phases (fig 7, A)
- e) Voluntary control exhibited prompt response with normal wave form except for an increase in electropotential and an increase in time of the B and C phases (fig 7, B)

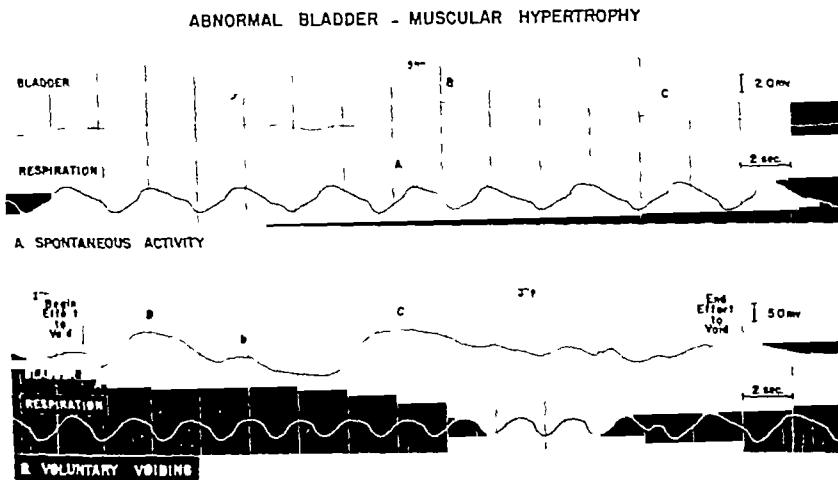


FIG 7 Examples of electromyographic records from bladder with muscular hypertrophy. 4, patient had early hyperplasia of prostate with slight trabeculation of bladder but without residual urine. Flat configuration of peaks of A and B phases is due to fact that electromotive force developed by bladder exceeded range of possible excursion of oscillographic needle. When this occurs during an examination, it is instantaneously corrected by of machine so as to bring changes in electromotive force within range (All amplification settings used during trace are calibrated in millivolts at end of examination.)

B, voluntary effort to void in same patient as 4. Note more rapid respiratory rate during effort to void and large electromotive force developed. (An excursion of oscillographic needle that is here equivalent to 5.0 millivolts is equivalent to 2.0 mv in A, and to only 0.4 mv in figure 6, 1 and B)

II Muscular degeneration (fig 8, table 1) All of these patients were demonstrated to have a "decompensated" bladder, as evidenced by cellule formation or diverticula, and usually with a residual urine of more than 60 cc. Twenty-three patients were included in this group, all of whom had urethral obstruction from either prostatic enlargement or urethral stricture. The following variations from the normal electromyogram were observed:

- a) Rhythm. Sometimes normal but usually characterized by prolonged periods of quiescence. The extended intervals between waves suggested complete absence of one or more waves.
- b) Wave form. Variations or irregularity in the basic normal pattern were

In the groups of 14 patients living 5 years or longer without recurrence, whose tumors had infiltrated up to halfway through the muscle, 8 lived 7 or more years (table 5). Four of these tumors had infiltrated the muscle and were among the most malignant ordinarily encountered.

Of the total group of 50 cases subjected to segmental resection prior to February 1, 1946, 9 patients died postoperatively. This operative mortality of 18 per cent is in line with the results in 80 patients with infiltrating carcinoma surviving operation prior to February 1, 1946.

TABLE 4 Results in 80 patients with infiltrating carcinoma surviving operation prior to February 1, 1946

SEGMENTAL RESECTION	CYSTECTOMY	Total	
		39	41
Lived 5 years or longer without cancer	6 (5, superficial)	7	3
	1 (1, deep)		
	26 (2, superficial)		
Died, or living, with cancer			
Died of other causes, within 5 years			

TABLE 5 Relation of survival to depth of infiltration, histopathology, and type of operation

SURVIVAL WITHOUT TUMOR (YEARS)	CASES	GROUP	HISTOPATHOLOGY	OPERATION
5	3	1	Well diff pap	Segmental
		1	Mod diff pap	Cystectomy
		1	Mod diff pap	Cystectomy
6	3	1	Mod diff pap	Segmental
		1	Mod diff pap	Segmental
		1	Mod diff pap	Segmental
7	3	1	Undiff ca	Segmental
		1	Mod diff pap	Segmental
		1	Well diff pap	Cystectomy
8	0	1	Mod diff pap	Cystectomy
9	2	1	Mod diff pap	Cystectomy
10	1	1	Mod diff pap	Cystectomy
11	1	1	Mod diff pap	Segmental
12	0	1	Mod diff pap	Segmental
13	0	1	Mod diff pap	Segmental
14	1	1	Mod diff pap	Segmental

cent occurred between 1928 and 1944, before the advent of antibiotics and the blood bank, and was confined to patients with Group C tumors, which had invaded the perivesical fat. The 3 patients who died in less than 5 years or were operated on between 1930 and 1942. One of these died of the tumor, one from cerebral emboli, and one from coronary occlusion.

In the corresponding cystectomy group, 7 of 16 patients died postoperatively.

ABNORMAL BLADDER - MUSCULAR DEGENERATION

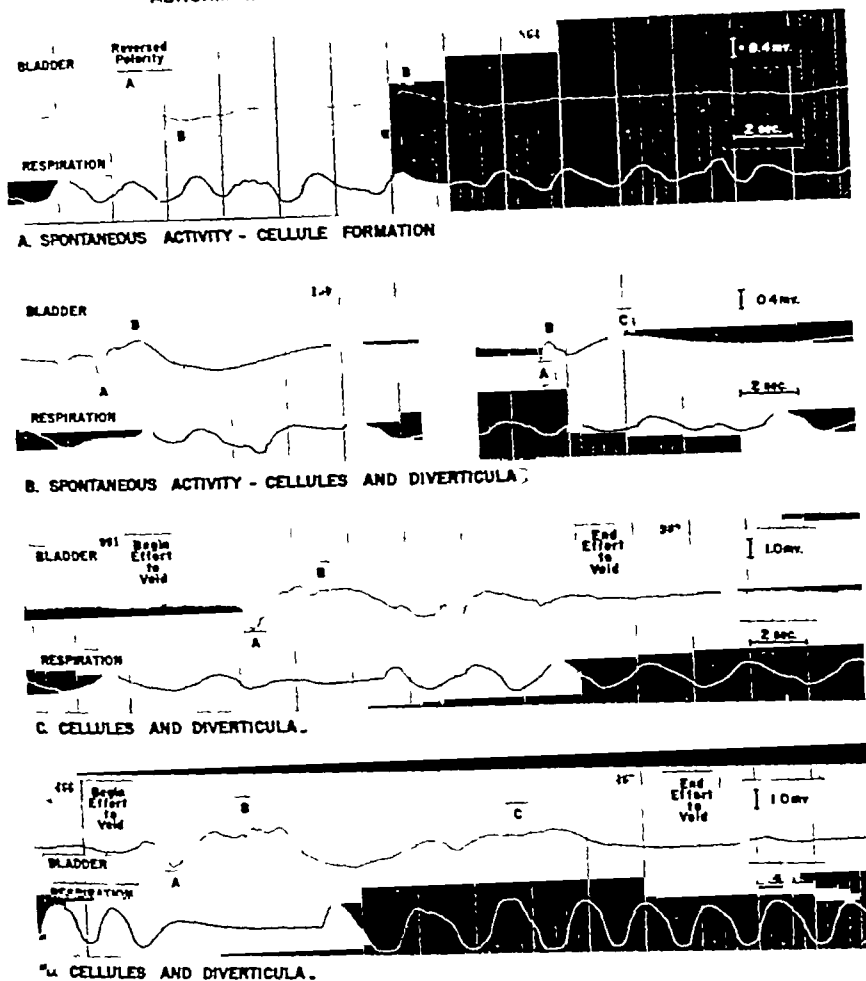


FIG 8 Examples of electromyographic records from series of bladders with muscular degeneration

1, patient with benign prostatic hyperplasia and atonic bladder with generalized early cellule formation. Note spontaneous reversal of polarity in first wave, that is, inversion of wave with A phase developing above base line, and B phase below base line.

B, spontaneous activity in bladder with many cellules and small diverticula. Note difficulty of determining presence of reversed polarity in this type of trace by inverting photograph and reading from right to left.

C and D, voluntary effort to void by different patients with many small diverticula and cellules. Note many small irregularities or minor oscillations of needle which distort trace in each of these records.

Note relatively low electromotive force developed in all of individuals as compared with figures 6 and 7 (mv scale in upper right corner).

Wave. If an electropotential approaching the normal was ever attained, there might be a reduction or "masking" of the changes listed in b and d above.

A striking and as yet unexplained phenomenon in many of these patients was

tinguish preoperatively between superficially and deeply infiltrating tumors, so that the survival rate in the superficial group can be accurately established and will not be needlessly reduced by the inadvertent inclusion in the series of many deeply infiltrating and incurable cases.

The clinical segregation of superficial from deep tumors is best accomplished by the correlation of the properly taken biopsy specimen with pelvic examination under anesthesia. A 3-dimensional mass, with sections showing tumor in the muscle layer, indicates deep infiltration. Simple induration of the bladder wall, with sections showing tumor in the muscle layer, practically always indicates a deep tumor, unless the induration disappears immediately after removal of the growth by transurethral electro-resection (fig. 2). If no induration can be felt by the experienced examiner and the tumor lies in a normally accessible location, infiltration, if any, usually will not be more than halfway through the muscularis.

CONCLUSION

Although basic principles probably cannot be established by an analysis of a small series of cases, the results herein reported strongly suggest that tumors, regardless of histologic pattern and degree of malignancy, which have infiltrated less than halfway through the muscularis usually are still confined to the bladder wall, and tumors which have infiltrated more deeply usually have spread beyond it.

The clinical segregation of these 2 groups not only enables us to determine the general outlook in any given case, but also provides a fairly stable basis for the subsequent measurement of the efficacy of different methods of treatment.

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a) Rhythm was quite slow. Spontaneous activity might be entirely absent but one or two waves usually occurred in a 15 to 20 minute record

b) Wave form was essentially normal (fig 9, A)

c) Electromotive force was usually decreased in all phases of the wave but approached the normal in some patients. The C phase tended to be markedly decreased or entirely absent

d) Time was reduced, especially in the C phase

e) Voluntary control was entirely absent

B The hyperactive neurogenic bladder. Seventeen patients were observed at intervals of 8 weeks or more after the initial spinal cord injury. All of these patients had demonstrated their ability to void at intervals of from a few minutes to 6 hours. Two individuals had been under constant observation from the time of injury, and had been followed from the hypoactive to the hyperactive type of bladder. Thirteen of the group complained of intermittent "bladder spasm," and all demonstrated a hyperactive type of record with the conventional sphygmometer.

a) Rhythm was very irregular and unpredictable with alternating bursts of rapid activity (fig 9, B) and long periods of quiescence

b) Wave form was essentially normal unless there was intrinsic muscular change. Marked trabeculation and cellule formation gave the superimposed changes listed as characteristic of "muscular degeneration" (fig 8, C)

c) Electropotential was characterized by marked variation not only in the various phases of individual waves but from one wave to the next. In the typical "bladder spasm" the phases were of enormous electromotive force (5 to 8 millivolts) in the B phase with many "b" waves. Such marked potential changes were accompanied by severe pain (fig 9, D)

d) Time increments varied in the same unpredictable manner as did the rhythm. With the development of very large potentials the duration was often relatively shortened. This was in contrast to the prolonged time factor that usually accompanied the elevated electropotentials of waves from the bladder with muscular hypertrophy (Compare figs 7 and 9, B)

e) Voluntary control was usually absent. When present, it varied in degree and was initiated with difficulty after repeated efforts. There was marked variation in electropotential, and in the duration of the different phases exhibited in successive efforts to void. The C phase was usually characterized by a series of potential changes of varying electromotive force and duration rather than by a single sustained elevation of the base line.

IV Pathologic conditions in which the record was variable and difficult to interpret. These have been limited entirely to neuropsychiatric patients, 19 of whom constituted this series. In general records from those patients who were agitated and aggressive gave evidence of a hyperactive bladder. In contrast, tracings secured from regressive patients indicated a more hypoactive type of bladder pattern. This did not apply in all cases, however. Patients with psychogenic sexual impotence, frigidity in the female, and the milder types of anxiety states have been observed to exhibit little or no spontaneous electropotential

Finally and as Dr Jewett will agree, we must not place too much emphasis upon statistics in cancer surgery. With our present limitations, it is not to be expected that they will be impressive because the doubtful cases must enter into the figures as well as the favorable ones and even the favorable ones may prove to have hidden metastases. Furthermore, we must not judge one method by comparison with another unless the conditions for which the two methods are employed are essentially the same. Each cancer patient must be given the best chance for cure, by whatever method and whatever the chance may be. I congratulate Dr Jewett for his very valuable contribution.

DR THOMAS J. KIRWIN (New York, N. Y.) I have followed Dr Jewett's work with keen professional and personal interest. At first I felt his views were too radical, but I have since changed my mind. My inclination has always been toward conservatism and in today's presentation I perceive a definite trend away from extremely radical measures.

Dr Jewett has again brought out the prime diagnostic importance of depth of muscular invasion of the bladder wall as a measure of the suitability of any given method of treatment for bladder tumors. He has shown that when a tumor has deeply invaded the muscle, the surgeon can look for no more favorable results from total cystectomy than from almost any other kind of treatment. Even under what are generally termed "good" conditions for operation, I would hesitate a long time before subjecting a relatively young patient—say, a man of 35 otherwise in good physical and sexual health—to perform a vesiculectomy, prostatectomy and cystectomy with bilateral ureteral transplantation. Even if the operation is perfectly successful, the man must remain unsexed and mutilated for the second half of his life. Neither would I ask a man of 60 or over to accept the operation when I can give him no guarantee that he will be cured and remain so for the few years of his allotted life span which is only 66.5 years provided he is a perfectly healthy individual who meets with no accident. We do not know the cause of carcinoma of the bladder.

I recall that last November Dr Colby read a paper in New York City, which I discussed, in which he stated that, if a tumor has not invaded the muscular wall of the bladder, segmental resection and local destruction have, in his experience, led to fewer fatalities than have cystectomies. Here accurate early diagnosis plays an important part. The cases recommended as suitable for cystectomy and ureteral transplantation are precisely those which will do best under conservative management.

A most excellent monograph on bladder tumors was recently sent me by the author, Curt Franksen of Stockholm. He stresses the importance of determining how far a tumor may have extended in the plane of the bladder wall for it often arises in the wall itself, and then usually extends to the deeper layers. This extension may not be visible on cystoscopy if there are no changes in the vesical mucosa. In some cases, however, erythematous patches and granules in the normal mucosa outside the tumor may suggest "tumor islands." These have a tendency to spread to the deeper layers and thus, the cystoscope will not reveal. However, Franksen has observed that the spread is in some degree proportional to the depth of the growth and also, to a certain extent, bears a relation to the grade of malignancy. The tissues are more rigid and by thus induration and

Such a concept is in complete accord with the observations in this series of patients. In any event, the simple water manometer experiments served to establish a close relationship between changes in intravesical pressure brought about by muscular contraction and the oscillographic recording of the electropotentials.

2) The B phase apparently occurs at the time of initiation of muscular contraction. This was quite clearly demonstrated by the water manometer, which showed simultaneous changes in intravesical pressure. On the basis of these observations one may assume that the A phase is associated with the spread of the excitation process and the B phase with the muscular activity. The diphasic character of the recorded A and B waves might thus be anticipated, since two electrodes were used. Indeed, the only way to obtain a monophasic wave with bipolar contact electrodes, as used in these experiments, would be to place one contact on an area of injured muscle which was capable of conduction but not of dipole formation and hence could not enter into the formation of an electric field.

3) The C phase, or sustained increase in negativity as demonstrated by elevation of the base line following the A and B phases, is considered to represent a sustained tonic contraction. This view is supported by the accompanying sustained elevation of the water manometer and by the steady flow of urine about the electrode carrier during voluntary efforts to void.

4) The strength of the electromotive force generated seems to be in general directly proportional to the mass of functioning muscle tissue involved. The high potentials demonstrated in early hypertrophy of the detrusor following urethral obstruction have been interpreted as evidence of this correlation. The low potentials observed in the "decompensated" bladder and in chronic bacterial or radiation cystitis of long duration lend converse support to this opinion.

5) The pathologic processes which are associated with muscular degeneration or interruption of muscular continuity were reflected in the record by interruptions in continuity, that is, distortion of the trace. This would seem to indicate interference with muscular conduction (fig. 8). However, the bladder wall containing cellulæ or diverticula offers a poor surface for constant electrode contact and it is difficult to be certain that these distortions do not represent artefacts due to changes in electrode-to-bladder contact during contraction. On the other hand, the presence of these distortions has been observed in the small contracted bladder following extensive x-ray and radium radiation for carcinoma of the cervix uteri in which no bladder cellulæ or diverticula were present. The presence of these distortions in the A phase, which seems to be purely a conduction phenomenon unassociated with muscle contraction, further indicates that such deviations from the normal are due to interference with conduction and are not mechanical artefacts.

6) The electropotentials observed are probably both too large and too sustained to be produced by the nerve tissue present in the bladder wall, and so are almost certainly of muscular origin. It has not been demonstrated that every smooth muscle cell in the detrusor receives an efferent nerve termination.

7) Injuries which involve bladder innervation but not bladder musculature result in changes in frequency, electromotive force, and duration of the oscillographic record but not in the basic wave form of the potentials as recorded by

ment of bladder tumors. It is believed that if total cystectomy is to be done for cure, it must be done radically, early, and in one stage. On the other hand, it is believed that as a palliative measure, total cystectomy is an excellent procedure and makes death from metastasis easier.

DR RUBIN H. FLOCKS (Iowa City, Iowa). I want to congratulate Dr. Jewett for the work which he has been doing with regard to the pathology of carcinoma of the bladder. His contribution has been certainly one of the most noteworthy in the last few years.

I had the opportunity of reviewing our cases that had been treated by transurethral resection and coagulation of the tumor base, and tried to study them on his basis.

In a group of 50 consecutive cases which would fall into Group B-1, as he classified them, there were 56 per cent five-year survivals. On the other hand, those that fell into Group B-2 showed a very negligible percentage of five-year survivals—approximately 3 per cent—so that this would fit in with his results. A larger group which was not analyzed in exactly the same way also fits in with his studies, this is a group of 200 patients treated in a similar manner.

Of those that fell into Group B-1, so far as we could tell clinically, none of these patients were explored, and in none of these patients did we have cross-sections completely through the bladder wall, so that there was a good chance for error. Those that fell into Group B-1 had a survival rate of 3.83 years. Every one of these patients was followed for 5 years or more.

Those that fell into Group B-2 had a survival rate of .75 years, and those that fell into another group—which he does not bring out in his paper—in which there was very definite invasion of the prostate, have a survival rate of 1.51 years.

I would like to ask him how many of his 80 cases had invasion of the prostate, and what happened to those patients.

DR JEWETT. In answer to the question raised by Dr. Graves regarding choice of treatment, I wish to emphasize that the two types of treatment reported in my paper were used simply to enable us to determine which sort of tumors had been confined to the bladder wall, and which sort had spread beyond the bladder wall prior to operation. Of all the different methods of treatment for tumors of the bladder which we used today, the most ideal has not yet been identified.

I should like to leave with you the idea that superficially infiltrating tumors for the most part have not metastasized, and are confined to the bladder wall, and radical procedures therefore are probably not indicated for them. Deeply infiltrating tumors, on the other hand, usually have spread beyond the bladder wall, and therefore cannot ordinarily be eradicated. It remains to be seen whether the more radical operations, such as pelvic exenteration, will lead to a better 5-year survival rate without causing an objectionably high incidence of postoperative disability.

With regard to Doctor Flocks's question, tumors which have invaded the prostate directly without first having grown down the prostatic urethra, fall into group C, since they have to penetrate the whole thickness of the bladder wall before reaching the prostate, unless the latter is hyperplastic and intruding intravesically. So far as I can recall, we have had no five-year survivals when the prostate has been invaded.

of factors 1) The smooth muscle studied in the various experiments was derived from a wide variety of animals and many different organs 2) The preparations were invariably in an artificial environment, traumatized and deprived of both blood and nerve supply This was true even in those instances in which studies were made *in situ* 3) Stimuli consisted of a galvanic current, mechanical trauma, or even sometimes the rhythmic contractions of isolated strips of smooth muscle The results of such investigations are of inestimable value as basic research, but it is obviously unwise to interpret the bioelectric potentials developed in the intact human bladder on the basis of observations made in the experimental animal It may, however, be remarked that the slow potentials demonstrated in the ureter of the experimental animal closely approximate in many respects those demonstrated in the human bladder in this series

Difficulties in interpretation of the electromyogram of the bladder stem directly from the paucity of information concerning the biophysical mechanisms by which these electrical phenomena are produced The interpretation of electromyograms of the bladder will undoubtedly be greatly modified by future developments in biophysics and by continued application of a technique similar to that herewith described to a large number of clinical cases, in which every available diagnostic procedure has been utilized to establish a correct diagnosis This has been the case with electrocardiography and electro-encephalography, which have developed almost wholly by the somewhat empirical method of clinical application and observation This report is therefore to be considered as a preliminary series of observations, and at present no strict interpretation of bladder function based on electropotential changes is implied, particularly if such interpretation should be at variance with well established methods of diagnosis

SUMMARY

Muscular activity of the intact human bladder is preceded and accompanied by electropotential changes which can be translated into characteristic wave forms by a suitable electronic technique

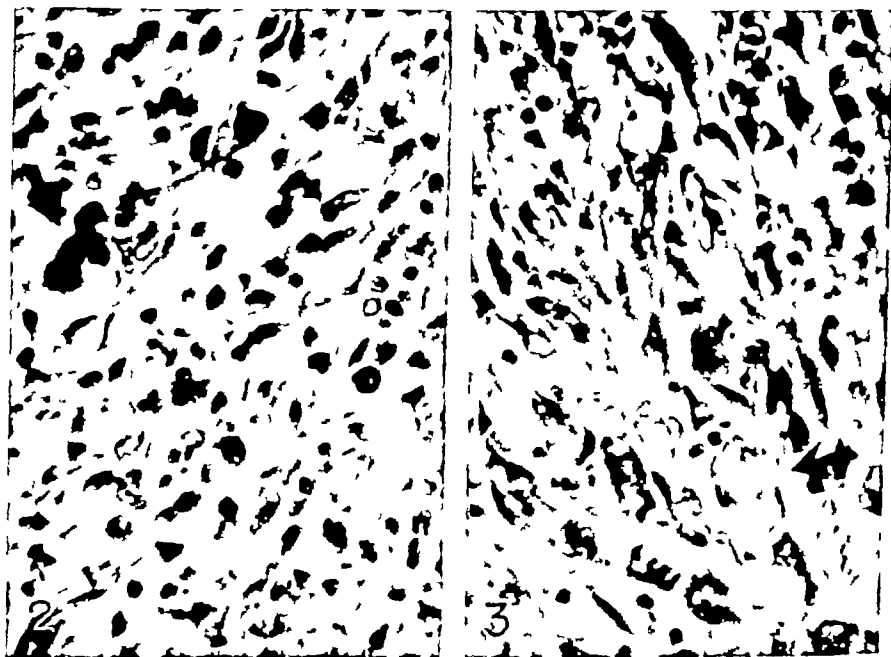
Under the conditions of these experiments spontaneous activity constantly occurs in the normal human bladder in the form of rhythmic contractions Voluntary activity of the bladder produces an oscillographic pattern similar in form to that of the spontaneous contraction and different only in the mechanical force exerted Injury to the bladder musculature or interruption of its nerve supply produces changes in the electropotentials as they develop, and these may be readily identified on the oscillographic record

It is therefore suggested that further development of this technique may result in a valuable addition to the diagnostic armamentarium of the urologist

The author would like to express his gratitude to Dr Samuel A Vest, who has provided not only the clinical and laboratory material for this study but whose inspiration direction and assistance have been invaluable in attaining these results

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Figs. 1, 2, 3

Fig. 1. Multiple polypoid masses completely fill bladder. AFIP Accession 26969.

Figs. 2 and 3. Microscopic appearance of tumor seen in figure 1. Cells of three types are identified. A spherical or oval cell with a small amount of cytoplasm surrounding a large vesicular nucleus intermingled with inflammatory cells; multi nucleated giant cells (arrow) and spindle shaped cells are also seen. AFIP Accession 26969.

hydronephrosis and pyelonephritis. In only one patient was metastasis to a regional lymph node observed. The only patient that is still living is one of the 2 on whom total cystectomy was performed within 4 months of the time of lesion

DISCUSSION

DR CHARLES B HUGGINS (Chicago, Ill) Dr Boyce is a true champion, appearing year after year and taking home the bacon I am quite sure that when it gets around that he is retired from the essay competition, the number of candidates will increase I understand the committee has already considered establishing a special first prize for Dr Boyce alone, so that the rest of the young men will have a little more even chance in the competition

This is a difficult field of electrophysiology, one of the many fields of which I know nothing It is true that people have been talking about these things for some years, it remained for Dr Boyce to do something about it

Electrophysiology, of course, is one of the most difficult fields of investigation, and one of the hazards is the so-called artefact

All I can do is ask Dr Boyce some questions In the first place, is he convinced that artefacts do not occur? In other fields of the body, presumably in the bladder, as well, there occur changes in potential between right and left homologous areas, frequently, and Dr Boyce has his electrodes on the right and left sides of the bladder How many of these wave changes are artefacts due to a shift in potential not associated with muscular activity?

I think it might be of great interest to make some observations with both electrodes on the same part of the bladder I would be particularly interested to see what sort of waves occur in eversion of the bladder, and I wonder if Dr Boyce has done that

One of the bugbears of the electrophysiologist, so I am told, is movement If the bladder contracts, it moves, and this, too, would give rise to artefacts It is the artefacts that worry me

I certainly think that this is a modest beginning in an important field of investigation, and I hope that Dr Boyce will be supported extensively in his studies I hope he will make many more studies, and continue to win prizes from year to year

DR BOYCE There certainly are artefacts potentially present in any field of electromyography Electropotential differences arise in nature in an almost countless variety of circumstances which may serve as sources of artefacts or aberrant electropotential differences encountered in recording action potentials from a single muscle mass such as the bladder Normal or abnormal electropotentials arising elsewhere in the body and entirely unrelated to the muscle mass being studied may be superimposed upon the record These should be termed "aberrant electropotentials" in contradistinction to mechanical interference which produces true artefacts I believe that we have succeeded in eliminating the majority of the aberrant electropotential differences" and "artefacts" which may interfere with the reliable interpretation of the record

The electropotentials from the heart have been entirely eliminated from the trace by placement of the surface electrode or "patient ground" in the midline of the abdomen When present, these appeared as the typical EKG pattern

was first noted, a recent report stated that he was well almost 4 years after the first operation.³

Pathologic observations Gross examination of the bladder showed multiple, soft, myxomatous, polypoid, grapelike clusters arising from the trigone, the bladder neck, the vesical orifice, and sometimes covering the entire inner surface of the bladder. The grapelike appearance is the most characteristic feature of the tumor and the only one which would justify its designation as *sarcoma botryoides*.

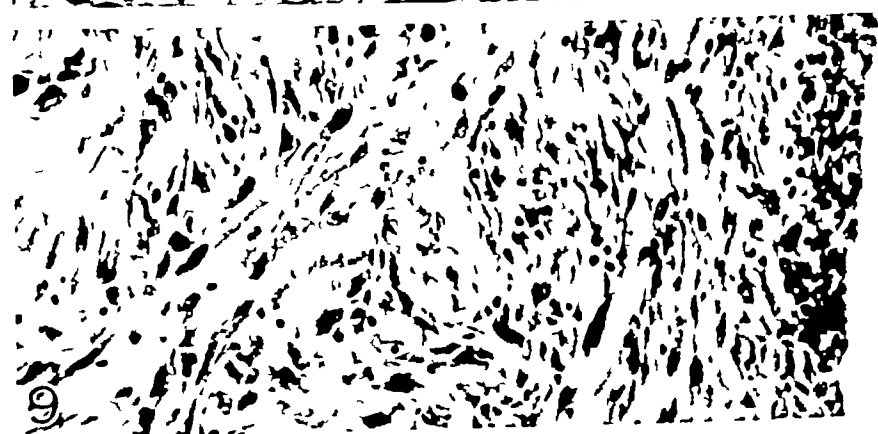
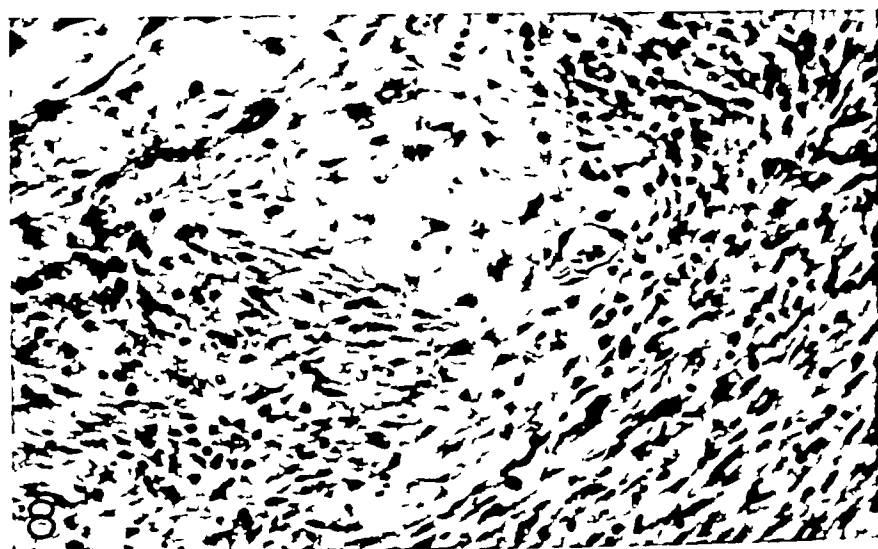
The histologic pattern of the tumor is shown in figures 4 to 9. The transitional surface epithelium may be intact (fig. 4), or ulceration and necrosis of tissue may occur. The lamina propria is replaced by myxomatous tissue containing stellate cells, and a few polymorphonuclear leukocytes, lymphocytes and monocytes (figs. 5, 6). Thus in superficial biopsies early in the disease the true nature of the lesion may be entirely masked by the sparsity of neoplastic cells and the presence of inflammatory reaction. In other cases squamous metaplasia of the surface epithelium and glandular formations may be found, simulating infiltrating carcinoma (figs. 4, 7).

The tumor may contain foci made up of interlacing bundles of slender, spindle-shaped mesenchymal cells with acidophilic cytoplasm, forming longitudinal fibers and surrounding an elongated hyperchromatic nucleus (fig. 8). These may alternate with myxomatous areas containing a scattering of monocytes, lymphocytes, and granulocytes.

Cells of three types have been described by Houette.⁴ The first type is a rather large spherical cell with a small amount of faintly acidophilic cytoplasm and a round or oval vesicular nucleus, quite suggestive of a lymphocyte except that the nuclear material is more clearly visible. These cells are the primitive or blastoma cells of Masson. They may display occasional mitotic figures. The second type consists of multinucleated giant cells in which a small amount of vacuolated or acidophilic cytoplasm surrounds from 5 to 20 small hyperchromatic centrally situated nuclei. The third type includes the more differentiated oval or spindle-shaped cells with eosinophilic cytoplasm, which may show longitudinal fibrils at one or both ends (fig. 9). Other cells may have both longitudinal fibrils and cross striations in their cytoplasm. These striated muscle cells, which are infrequent in the superficial portions and in the tissue removed early in the course of the disease, become more abundant in the deeper portions and in tumor tissue removed later in the disease.

It should be emphasized that the characteristic microscopic picture in the early stages of the disease is that of a loose myxomatous tissue through which spindle-shaped cells and varying numbers of inflammatory cells are scattered. Some of the spindle cells may show cross striations. This loose edematous tissue gives rise to the grapelike appearance of the tumor, justifying the use of the term *sarcoma botryoides* to differentiate these tumors from other rhabdomyosarcomas. The three cell types that have been described appear in later stages of the disease when the striated muscle cells can usually be found with ease.

⁴ Houette, C. *Ann d'anat path.* 6: 267-282, 1929.



FIGS 7, 8, 9

FIG 7 Gland like inclusion of surface epithelium (arrow) simulates carcinoma AFIP Accession 64201

FIG 8 Foci of spindle shaped cells alternate with loose myxomatous areas $\times 200$ AFIP Accession 56319

FIG 9 Spindle shaped cells are predominant $\times 200$ AFIP Accession 235129

treated by cystectomy, principally because they suffered fewer complications after discharge from the hospital (table 4) In each of these 2 groups there was

Non-infiltrating		Cases		Living 5 to 14 years without tumor	
Superficial	Group A	Submucosa	14	10	
	Group B1	Muscle	5	4	
Deep	Group B2	Perivesical tissue	13	1	
	Group C	and Lymphatics	48	1	

FIG 1

TABLE 1 Results of complete extirpation of primary growth in 80 patients surviving operation prior to February 1 1948

SURVIVAL	LIVED TO 14 YEARS WITHOUT TUMOR		DIED WITH TUMOR OR LIVING WITH TUMOR		DIED IN LESS THAN 5 YEARS FROM CAUSES OTHER THAN TUMOR	
Group	Superficial	Deep	Superficial	Deep	Superficial	Deep
Well diff pap ca	2					
Mod diff pap ca	5	1	2	8	3	1
Sl diff pap ca	1	1		2		1
Mod diff epid ca	2			10		2
Sl diff epid ca	3			19		2
Undiff ca	1			8		1
Adenocarcinoma				2		
Mucus cell ca				3		
Total	14 (74%)	2 (3%)	2 (10%)	52 (85%)	3 (16%)	7 (12%)

TABLE 2 Comparison of histologic pattern in surviving group with that in group living or dying with tumor

	LIVED 5 TO 14 YEARS WITHOUT TUMOR	DIED WITH TUMOR OR LIVING WITH TUMOR
Pap carcinoma	10 (63%)	12 (22%)
Epid carcinoma	5 (31%)	20 (54%)
Undiff carcinoma	1 (6%)	8 (15%)
Adenocarcinoma		2 (4%)
Mucus cell carcinoma		3 (5%)

TABLE 3 Comparison of degree of malignancy in surviving group with that in group living or dying with tumor

DEGREE OF CELLULAR DIFFERENTIATION	LIVED TO 14 YEARS WITHOUT TUMOR	DIED WITH TUMOR OR LIVING WITH TUMOR
Sl diff ca	5 (31%)	21 (39%)
Undiff ca	1 (6%)	8 (15%)
Total	6 (37%)	29 (54%)

only 1 patient with a deeply infiltrating tumor who was alive and free of cancer after 5 years

PRIMARY SARCOMA OF THE BLADDER IN CHILDREN A REPORT OF TWO CASES

ROGER A WAY

Primary sarcoma of the bladder in children is uncommon. Denning in 1921 collected 64 authentic cases in the first decade of life, 18 of which were 2 years old or younger. In 1949 Henry found 89 recorded cases and reported 2 additional ones.

The symptoms depend upon the location of the tumor, the rapidity of its growth and the presence or absence of infection. Symptoms of bladder obstruction may result from involvement at the vesical neck or reduction of elasticity or capacity from generalized infiltration of the bladder wall. Renal failure, frequently rapid, may result from obstruction of the intramural portions of the ureters. Pain is generally confined to the hypogastric region and the external genitalia. Infection is prone to develop early. Gross hematuria is uncommon. Abdominal distention and difficult defecation from pressure on the large bowel, edema of the lower extremities from venous compression and pain from pressure on the pelvic nerves may develop late. Priapism has been attributed to irritation of the nervi erigentes. In female children the tumor has been known to prolapse through the urethra. Hunt observed a child with sarcomatous vesical neck obstruction at birth in which the urachus opened on the nineteenth day of life with a discharge of urine.

The diagnosis of vesical sarcoma is difficult at a stage when therapy is effective. Frequently the patient is not seen until the late stages. Symptoms are overlooked or often do not develop until the tumor is far advanced. In those cases in which an operable lesion is present diagnosis is difficult since the lesion begins in the submucosa and usually involves the mucosa of the bladder late or not at all. Very rarely, when the tumor invades the mucosa, a diagnosis by cystoscopic biopsy is possible. Cystography reveals not only the gross abnormalities in the cavity of the bladder but also fixation of the bladder wall. In the late stages a hard suprapubic mass may be palpated and induration and fixation of the floor of the bladder are often noted on rectal examination.

In differential diagnosis vesical calculi, foreign bodies within the bladder, urinary tract infection, obstruction from embryological defects or neurological dysfunctions, as well as abscess or sarcoma of the prostate, must be considered. Vesical carcinoma need not be considered, since no case of malignant epithelial tumor of the bladder in children has been reported.

Although lymphatic, osteogenic and neurogenic sarcoma as well as tumors of mixed cellular elements have been recorded, the majority of the 91 reported cases have been classified as fibrosarcoma or myosarcoma. In the early stages the tumor is small, single, and fairly well localized in the submucosa and by rapid invasion may develop in two directions: 1) It may infiltrate the entire bladder wall and extend to the surrounding tissues without breaking through the bladder mucosa.

Read at annual meeting, Southeastern Section, American Urological Association Memphis, Tenn., March 9, 1951.

between 1940 and 1944, giving an operative mortality of 15 per cent. Six of these patients had Group C tumors. Of the 7 patients who died in less than 5 years from causes other than cancer, 4 died from pyelonephritis (2, with initial cutaneous ureterostomies), 1, from self-induced hemorrhage following insertion of ureterostomy catheter, 1, from uremia, and 1 from hypertension and cardiac failure. These 7 patients were operated on between 1936 and 1945.

If the findings in this relatively small series of 80 cases are truly representative of the behavior of bladder tumors in general, it becomes a matter of the utmost importance to distinguish preoperatively between the superficially and the deeply infiltrating groups. Tumors which are deeply infiltrating, with metastases, usually

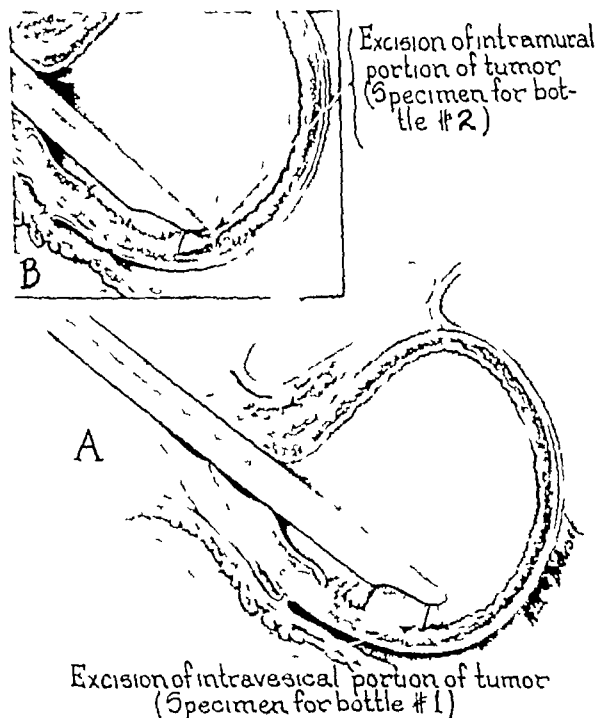


FIG. 2

cannot be eradicated by conservative procedures, although some of these methods may be useful for purposes of palliation. It remains to be seen whether more radical operations, such as radical cystectomy with resection of the lymphatic pathways, and pelvic exenteration will offer a more satisfactory survival rate in cases of deeply infiltrating tumors, without the high incidence of postoperative disability.

Tumors which are superficially infiltrating, without metastases, may be eradicated by simple extirpation, and therefore should not require a radical operation. It furthermore is possible that such tumors may be completely eradicated by local destruction with radium, or by electrocoagulation. To ascertain this, however, it becomes necessary

portion of the posterior wall, and the distal three fourths of the anterior wall (fig 1)

Renal function did not improve on catheter drainage, genital swelling increased, and 2 weeks after admission, edema of the left leg developed. Uncon-



FIG 1 Case 1. Lateral cystogram showing large, lobulated filling defect involving floor of bladder, distal portion of posterior wall and distal three fourths of anterior wall.



FIG 2 Case 1. Autopsy specimen showing marked dilation of renal pelvis and ureters with tumor filling bladder, most abundant in region of trigone. Edematous, grape-like masses are prominent. Trigone not distinguishable in tumor mass.

trollable abdominal distention and vomiting marked his progressive decline and death 1 month after admission.

At autopsy both kidneys were found to be enlarged with marked dilation of the pelvis and thinning of the cortical substance (fig 2). Both ureters were extremely dilated as far down as the ureterovesical junction, measuring 3 cm in diameter. An irregular, extraperitoneal mass containing the bladder filled the

DISCUSSION

DR ROGER C GRAVES (Boston, Mass.) I have great respect for Dr Jewett's experience and for his logical mind. I believe that he has proved his point to which he first called attention several years ago when he stated that the depth of penetration of a bladder tumor within the bladder wall has important prognostic significance. Like so many things that are true, this is entirely reasonable. For a long time we have known that prognosis is influenced by the grade of malignancy of the tumor. More important probably, in its effect upon the outcome of the case, is the depth of penetration in the bladder wall. Dr Jewett has shown that the 5-year survival rate is relatively high in the case of tumors with superficial infiltration of the muscularis, and very low in the case of those tumors with deep penetration. To determine this point one way or the other in the initial appraisal of the patient, he has stated that it is necessary to obtain adequate biopsy material and to examine the bladder region under anesthesia. The adequate preoperative biopsy is not so simple as it sounds and perhaps not so important. If this is essential it will be necessary to develop an instrument, more suitable than the resectoscope, which will obtain transurethrally a truly representative specimen of the tumor including a portion of its base. I hesitate to traumatize a cancer in this way. I prefer to learn the depth of infiltration by rectal palpation and from the final pathological report. In order to obtain a final report that will be significant in this regard, pathologists must be taught to make this particular observation as a part of their routine study.

There is no doubt that rectal examination under spinal anesthesia is essential in the preoperative study of a case of bladder tumor. The relaxation thus afforded permits careful bimanual palpation of the bladder and the pelvis which will determine, as Dr Jewett has stated, the extent of penetration by the tumor in the bladder wall. Rectal and pelvic examinations without anesthesia are of little value in the study of bladder neoplasms.

One more prognostic point which may be mentioned. It is the report of the pelvic lymph nodes included in the surgical specimen in cases of total cystectomy. When positive nodes are found the prognosis will be unfavorably affected.

I agree completely with Dr Jewett concerning the prognostic significance of the depth of infiltration by the tumor in the bladder wall. I differ with him somewhat concerning the emphasis to be placed upon this point in determining the plan of treatment. I believe that the choice of the method of treatment to be employed in the given case depends upon the extent of the tumor and its location in the bladder more than it does upon the grade of malignancy or the local depth of penetration. For example, I believe that tumors of the dome and anterior wall of the bladder lend themselves well to wide surgical resection. I believe that papillary and even small infiltrating tumors of the base of the bladder and lower lateral walls can be controlled well by electrocoagulation and radium applied through suprapubic cystotomy and that this is a better cancer operation than segmental resection in this region. I believe further that there are certain other tumors which, because of their extent and location and apart from their grade of malignancy or depth of penetration, require total extirpation of the bladder itself.

much straining. The stools were ribbon in character, and the urinary stream a mere dribble. There had been an indeterminate weight loss since the onset of the illness.

Physical examination revealed a well developed and well nourished healthy child. The abdomen was markedly distended and tympanic throughout. The bladder was extended to the umbilicus. Ten ounces of urine were removed by catheter, and a hard, irregular, suprapubic mass, extending some 6 cm above the symphysis pubis, was palpated. The external genitalia were not unusual,

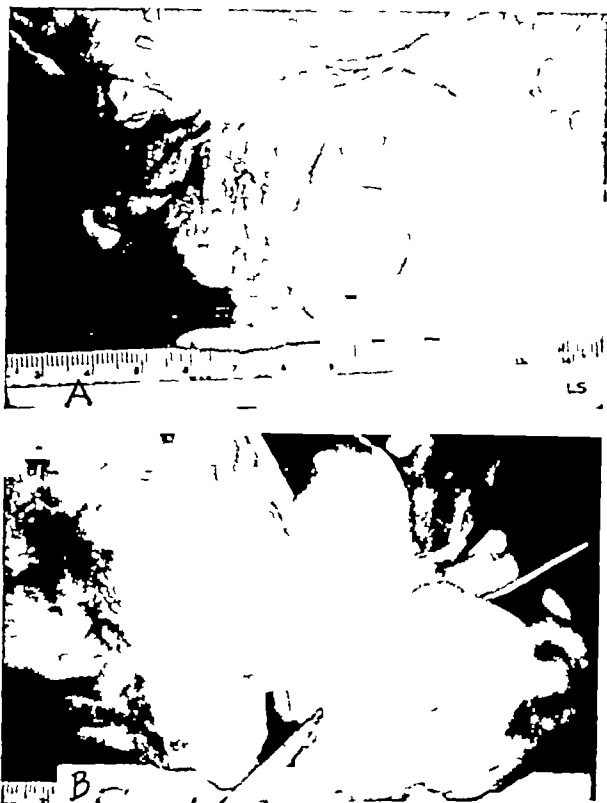


FIG 4 Case 24, solitary metastasis involving lesser curvature of stomach. Tumor infiltrated from outer wall to muscularis mucosa and mushroomed mucosa into lumen of stomach. B, autopsy specimen showing extensive infiltration of tumor into interior wall of bladder. Trigone and ureteral orifice not involved.

although urine dribbled intermittently from the penis. Rectal examination showed an indurated mass filling the pelvis.

Laboratory studies showed normal hemogram, blood urea nitrogen, and sedimentation rate. The urine was sterile and contained 1 to 3 blood cells per high powered field.

X-ray of the chest showed multiple round, metastatic lesions in the right lung and a single metastasis in the left. The patient died 6 days after admission. His hospital course was characterized by nausea and vomiting and intractable abdominal distention and progressively increasing fever, reaching 109°F prior to death.

thickening the effect of the tumor's spread can be fairly estimated. This author uses and recommends Jewett's method of bimanual palpation under anesthesia. The presence of all large tumors that invaded muscular wall may be detected by this means. The infiltration in the muscularis when palpated is a soft-to-firm mass and infiltration in the perivesical tissue is a firm-to-hard mass. Fixation to adjacent tissues can be determined in the same way.

Dr. Jewett's suggestions as to better diagnostic procedures, as well as the exact information he has furnished us on the histology and pathology of these bladder growths, constitute a very notable contribution to the solution of this vexed problem of the management of vesical neoplasms. He has definitely advanced an important branch of urologic practice.

MAJOR EVAN L. LEWIS (Washington, D. C.) At Walter Reed Army Hospital, all methods of treatment are used for carcinoma of the bladder, the procedure most applicable to the patient is used.

One particular method which is relatively new and has given good results is presented here. This technique of Friedman and Lewis (the *Walter Reed Technique*) entails the use of radioactive substance in the lumen of a Foley bag catheter, distending the balloon with a colored medium to a diameter of four centimeters and thereby delivering a dosage of 8000 gamma roentgens to the lower two-thirds of the bladder—the most frequent site of tumor.

This is particularly useful in preventing recurrence in the superficial tumors which have recurred previously.

Thirteen patients have been treated at Walter Reed Army Hospital since July 1945. These cases may be summarized as follows: 8 patients had recurrent tumors, 5 primary, 6 patients had multiple tumors, one as many as 13.

Pathologically, eleven were papillary, nine were grade 2, two were grade 3, one was grade 3 undifferentiated, one was grade 3 epidermoid. According to the classification of Jewett, there were group A, 6, group B₁, 4, group B₂, 2, group C, 1.

Supplemental treatment at the time of insertion of the radioactive element was suprapubic cystotomy and resection, 2, transurethral resection, 4, transurethral biopsy and fulguration, 7.

Gamma roentgens delivered to bladder wall 5,260–11,000 with an average of 8,200. Reactions varied from mild to severe, but all symptoms disappeared in 6 months or less. It is imperative that a check be made daily by instilling 30 cc Skiodan into the bladder, allowing it to drain out and taking an x-ray. The recurrences that have been found after radiation therapy have been due to sections of the bladder receiving less than required radiation.

Follow up: All patients are at present without tumor.

Without any recurrence, 9 patients: 6 years, 1 case, 5 years, 4 cases, 4 years, 1 case, 2 years, 1 case, less than 1 year, 2 cases.

Patients with recurrence: One recurred 2 years after radiation, in the dome, now is 3 years without tumor. One recurred 7 months after radiation, in the dome, now is 14 months without tumor. One recurred 4 months after radiation, in the lateral walls, necessitating total cystectomy. One recurred 3 weeks after radiation, in the dome, no tumor in 4 months.

Again it should be stressed that all standard methods are used for the treat-

RHABDOMYOSARCOMA OF THE URINARY BLADDER A FOLLOW-UP NOTE

HERMAN J. MEISEL, WILLIAM H. HEATH AND JOSEPH M. MILLER

From the Veterans Administration Hospital, Fort Howard, Md

In a previous communication in this journal (p. 525, March 1949) details of an instance of rhabdomyosarcoma of the urinary bladder were reported. This was the tenth such account published. These neoplasms are rapidly growing and quickly fatal, the longest survival period after diagnosis being 13 months and the average 6.5 months. Remote metastasis was found only once since the typical mode of growth is by direct extension and invasion. In the present instance, partial cystectomy was done on January 24, 1947. The patient died of an unrelated disease on November 4, 1948. Postmortem examination performed by the medical examiner did not show local recurrence or metastasis. This period of survival of 21 months is longer than has been previously reported. Except for an unconnected illness, permanent cure would have resulted.

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

POLYPOID RHABDOMYOSARCOMA (SARCOMA BOTRYOIDES) OF BLADDER IN CHILDREN

F K MOSTOFI AND W H MORSE, CAPT, MC, USA

From the Armed Forces Institute of Pathology, Washington, D C

A case which had been variously diagnosed as polyposis, squamous cell carcinoma, and fibroma of the bladder came to our attention during a review of the material in the Bladder Tumor Registry

This case was registered at the Army Medical Museum in 1863 by Dr Middleton Goldsmith, who had been Professor of Surgery and Dean of the Louisville, Kentucky, Medical School In the accompanying letter the contributor identified the specimen as a bladder from the body of a child who had died with symptoms of ammoniaemia, i e, uremia, and he rightfully claimed that it was one of the finest specimens of its kind in any museum

The bladder, which is at present on exhibit at the Medical Museum, is small and is filled with many polypoid masses of soft myxomatous tissue, measuring from 0.5 to 3 cm and arising from the bladder neck (fig 1) Microscopic sections show a polypoid tumor covered in areas by keratinized stratified squamous epithelium In the cellular areas of the stroma, cells of three types are recognizable (figs 2 and 3) The first are cells with pale vesicular nuclei, the second are multinucleated giant cells, and the third are spindle cells in some of which cross striations are detected In other areas the stroma is infiltrated with lymphocytes, polymorphonuclear leukocytes and monocytes Some of the sections consist of necrotic tissue

On the basis of the pathologic examination of the tissue a diagnosis of sarcoma botryoides or grapelike rhabdomyosarcoma of the bladder seems to be justified

DISCUSSION

Analysis of Registry cases The published cases of rhabdomyosarcoma of the bladder occurring in children have been adequately reviewed by Deming¹ and by Khoury and Speer.² In the Bladder Tumor Registry are records of 10 cases coded as sarcoma botryoides 2 of which may be found in the literature.^{1, 2} A detailed analysis of the clinical data relative to these Registry cases is given in table 1 Briefly, the patients ranged from 5 weeks to 9 years of age, and the symptoms consisted of dysuria, retention, hematuria and irritability The initial treatment consisted of excision with or without fulguration In every instance there was recurrence of the tumor (in most of the cases within 4 months after the first treatment) and all but one of the patients died within 24 months of the first operation The causes of death were local recurrence, cachexia, uremia,

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or the policy of the Veterans Administration

¹ Deming, C I. *Surg., Gynec. & Obst.* 39: 432-442, 1924

² Khoury, F N, and Speer, F D. *J Urol.* 51: 505-516, 1944

³ Flocks, R H. To be published *J Urol.*

TABLE 1

AGE	DIAGNOSIS	ACU	TREATMENT TRIED WITH RESULT	OPERATION & DATE	COMPLICATIONS	RE- SULT
Structure L. S.	Caliber 22	75	Prostate resected in Clin cal in '36 & '37	Resected 2 structures and some prostate '37	15 gm prostate	Fair No further sound Died 5 years later
Structure of urethra com- plete retention	W P S	16	Edforms to 18 Ret cath No 12 Bougie or sounds 170 times	Resected 3 areas of struc- ture '45	Grade 2 hyper prostate	Poor Caliber 18
Structures Complete reten- tion	H R	13	Edforms & ret cath Bougie & sounds 135 times	Resected 2 structures in Jan '47	Extimal urethrotomy	Excellent Caliber 24
Structure Caliber 16 Pcp in ulcer	M L	52	Dilatation frequently fol- lowed by severe chills and fever	Resected 1 structure & bar in Oct '44	Medium bar	Excellent Caliber 26
Structure & B P H	L P	60	Sounds by local M D	Resected 1 structure & prostate in Feb '50	Prostate Grade 3	Most obstruction was prostate Caliber 24
Ca of prostate and mul- tiple structure of urethra	N I G	77	Dilatation of structure for over a year No 18 light	Resected 3 structures & prostate in July '50	Ca of prostate Symptom less	Good result Caliber 22

TABLE 1 Clinical data from 10 cases of sarcoma botryoides of the urinary bladder in children

AGE SEX	SYMPTOMS	POSITION AD- MISSION DATE	CYSTOSCOPIC APPEARANCE	TREATMENT	LOCAL RECURRENT	METASTASIS	COURSE	CONTRIBUTOR
1 yr F	Urinary		Unknown			0	Died before 1863	Dr M Goldsmith, Louisville Ky
2 yr 10 mo F	Dysuria few days	10/7/17	Polypoid infiltration posterior wall above trigone	Excision fulguration radiation	1 month	0	Died 1/1/18 of recurrence hydromphrosia	Dr J J Clark, Syracuse N Y
2 yr 10 mo M	Retention few days	12/10/17	Large pedunculated cystic grape like masses outside left side	Excision marsupialization	8 days	0	Died 7/22/18 of recurrence hydromphrosia	Dr Sturgis, Milwaukee Wis
6 yr 10 mo M	Hematuria dysuria, frequency 3 months	3/1/22	Chalchous myxomatous polypoid mass trigone, ant & lat walls	Resection radiation	10 days	0	Died 2/10/13 of recurrence, hydromphrosia	Dr Donning New Haven, Conn
1 yr 10 mo F	Hematuria, sperm and frequency 5 months wt loss	1/9/18	Polypoid growth multiple soft fleshy homogeneous	Resection	1 month	+	Died 9/10/38 of recurrence hydromphrosia	Dr Barnes & Dr Bergman, Los Angeles, Calif
5 yr 10 mo M	Dribbling retention, dysuria 1 month	5/15/40	Polypoid ulcerated multilobed grape like ant wall above sphincter	Excision	3 months	0	Died 7/11 of recurrence ecchymosis	Dr Hall & Dr Thomas, Clarksburg W Va
1 yr 10 mo M	Hematuria few days	9/11/18	Polypoid large to pen size growths trigone and vesicle neck	Fulguration, cystectomy excision	Immediately	0	Died 9/18 of recurrence, hydromphrosia	Dr Morgan, Philadelphia Pa
2 yr 10 mo M	Hematuria dysuria 2 months, passed blood	1/10	Pedunculated mass of polyps internal urethral orifice	Excision total cystectomy	3 1/2 mos	0	Living and well May 1950	Dr R H Locke, Iowa City, Iowa
1 yr 10 mo M	Dysuria straining abd pain	5/48	Polypoid fleshy like tumor ant & post bladder neck	Excision total cystectomy	Date unknown	0	Died 5/9/19 recurrence	Dr A J Dean New York N Y
2 yr 10 mo F	Irritability perhaps immature	5/10/17	Nodular grape like cystic papillary mass, post wall of urethra	Excision fulguration, x ray	Date unknown	0	Died 7/25/19 of recurrence, hydromphrosia	Dr M Baker, Akron, Ohio

NEW SURGICAL PROCEDURE FOR CURE OF SCROTAL HYPOSPADIAS GRAFTING OF A MALE HUMAN URETHRA TAKEN FROM A FRESH CADAVER

J P BOURQUE

From the Department of Urology, Hotel Dieu Hospital, University of Montreal, Montreal, Canada

The multiplicity of surgical techniques that have been devised for the correction of hypospadias, especially when scrotal, shows to what extent the problem is known to be delicate and complicated

We had the occasion to observe an adult patient, M P, a white man, 19 years of age, born with a scrotal hypospadias. He was hospitalized in our service at the Hotel Dieu Hospital (Chart No 8434) in November 1946, and in his case we thought that we could get good results by grafting a human urethra taken from a fresh cadaver.

All the details of the description of the malformation will be omitted as we refer you to the photographs (fig 1). The only particularities to notice are the accentuated curvature of the penis and the situation of the abnormal urethral meatus on the median line, 1 to 2 cm lower than the penoscrotal angle.

METHOD OF OBTAINING AND PRESERVING THE GRAFT

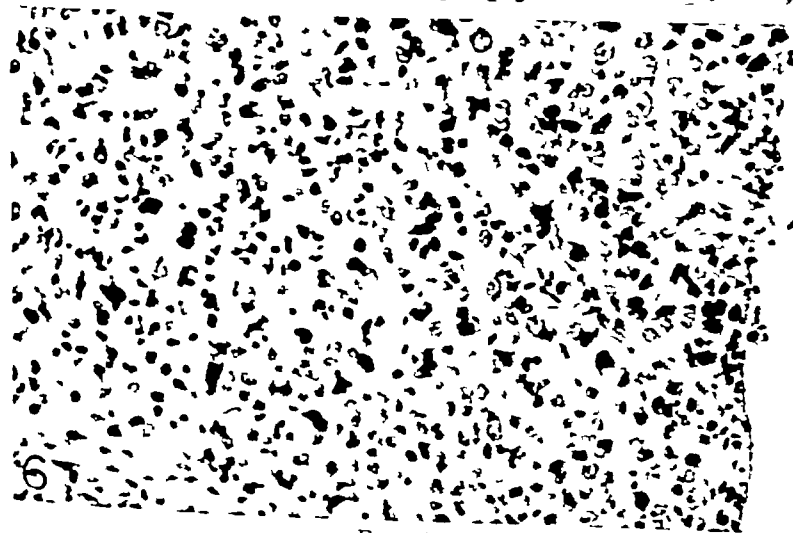
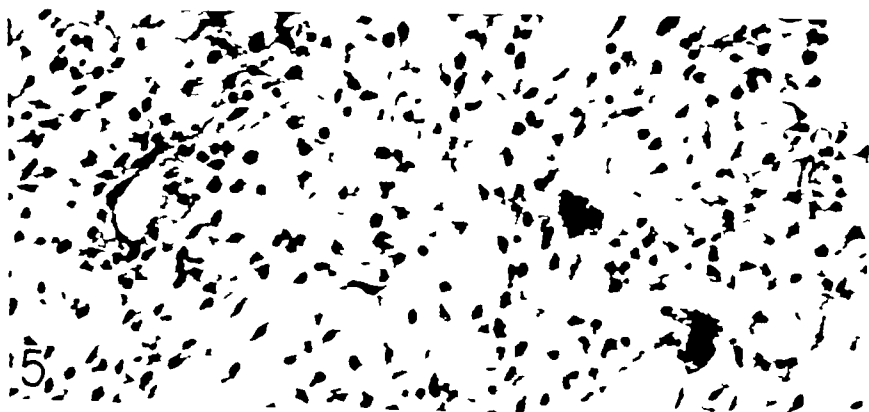
On a fresh cadaver, at the autopsy, 2 hours after death, we removed aseptically the whole of the urethra less the prostatic portion. This urethra was then mounted on a glass rod and placed in a bath of 95 per cent ethyl alcohol and left there (fig 2).

Four days later, 12 hours before the operation, the urethral graft was placed in an isotonic saline solution added with 1 000 000 units of penicillin and streptomycin, this being done in order to rehydrate the tissues which had been dehydrated and hardened by the alcohol and also to render them soft and easily manipulable.

OPERATIONS

In the first operations performed in November 1946 and in February 1947, we proceeded with the usual technique to correct the abnormal curvature of the penis, i.e. the resection of the fibrous band or chordee accentuating the abnormal curvature of the penis and forbidding normal erections. As this band was considerable, we decided to make this correction in two stages to obtain better results.

The patient was hospitalized again in September 1947, and, as the tissues of the penis were well healed and soft, we proceeded with the grafting by a modified Josselyn's tunnelization procedure. An incision was made around the urethral orifice, extended 1 cm below and above the abnormal meatus, dissection of the urethra on a length of 2 cm (fig 3, 1). From that point, with trocars of different calibers, that is from 14 to 24H (Charrière), we made a tunnel under the skin of the penis, between the two corpora, through to the glans penis, B. The tubular



FIGS 4, 5 6

FIG 4 Surface covered by squamous epithelium. Lamina propria is edematous and contains occasional stellate cells $\times 230$ AFIP Accession 230128

FIG 5 Small cells with scanty eosinophilic cytoplasm surrounding hyperchromatic nucleus. Occasional cell has a one or two pointed end $\times 230$ AFIP Accession 57162

FIG 6 Ulceration is present. Tumor is pleomorphic $\times 230$ AFIP Accession 63459

of the distal urethra and the graft, we closed the skin incision with Galli tubes and wire sutures (H) to assure compression and a good healing

FOLLOW-UP NOTES

The postoperative course was uneventful. On the seventh day, the catheter was removed and so were the wire sutures. There was a slight degree of sup-puration at the point of junction of the graft and of the new urethra which healed well, but the patient was left with a small fistula, 2 mm in diameter. The graft was not eliminated and healed well in place. The patient was then discharged and asked to come back 6 months later. When he left the hospital, he could urinate normally and the cystostomy wound was healed up completely.

In February 1948, the patient was rehospitalized and we operated on the urethral fistula which was left following the anterior operation.

The results have not been perfect but the patient has only a small fistula of the diameter of a No. 22 needle. This fistula does allow at times very little oozing



FIG 4 A, small fistula visible B, New urethral orifice at tip of glans penis

of urine during urination, sometimes a few drops but this does not happen is long as the patient puts his finger on the fistula while urinating. Erections are normal and the patient is happy.

For the late results, we refer you to figure 4, taken after the last operation was performed. The small fistula is barely noticeable.

The patient refused rehospitalization for the correction of the fistula because he feels well and would rather keep this small fistula than go through another operation.

RESULTS

As far as the functional point of view is concerned, the results are good, and as far as the esthetic effect is concerned, it is still better, because, as can be seen on the photograph, the penis is hardly without any scars, as is often the fact with other techniques. The penis is also without any abnormal curvature and erections are normal.

CONCLUSIONS

To our knowledge, after a thorough survey of the whole attainable literature on the problem, the foregoing procedure has never been performed previously.

Histogenesis The tumor is considered to arise from an embryonic tissue capable of differentiation into myxomatous tissue, fibrous tissue, and striated muscle. Histologically, the tumor may consist predominantly of one or any combination of these cell types. In its most differentiated form the tumor shows unmistakable striated muscle.

Historical review Khoury and Speer,² after an extensive search of the literature, found that the earliest reported case of rhabdomyosarcoma of bladder in a child was that of Mönckberg³ in 1907. We have not been able to find any earlier report. While Goldsmith made no formal report at the time, it is possible that this case of rhabdomyosarcoma of bladder in a child was the earliest to be confirmed by microscopic examination.

Three other early reports present clinical features and gross descriptions characteristic of this tumor. Crosse in 1830-35, Stanley-Savoy in 1852, and Brickett in 1857, each described polyposis of the bladder in a child—a boy less than 2 years of age, a 1 year old boy, and a 5 year old girl, respectively.⁶ All 3 patients died in a short time, the first from exhaustion after operation and the other two from kidney disease. Although microscopic proof is lacking, grossly the lesion was a polypoid tumor of the bladder and, since polypoid rhabdomyosarcoma is the most common bladder tumor in children, in the absence of evidence to the contrary, these cases may be so classified.

SUMMARY

A polypoid, grapelike tumor of the bladder removed from a child before 1863 has been examined microscopically, with evidence to permit its classification as polypoid rhabdomyosarcoma (sarcoma botryoides) since it resembles other similar cases reported in the literature.

Analysis of the 10 cases of polypoid rhabdomyosarcoma in the Bladder Tumor Registry shows that the lesion recurred almost invariably within 4 months and terminated fatally within 24 months.

Clinical and pathologic recognition of the lesion in its early phases is imperative if any hope for cure is to be entertained. The prognosis should always be guarded.

³ Mönckberg, J. G. *Virchows Arch f path Anat* 187: 471-516, 1907.

⁶ Brickett, J. *Royal Med & Chir Soc London*, 41: 311-321, 1858-59.

CARCINOMA OF THE PENIS

JULIO E. COLON

From the Hospital of Oncology and Institute of Radiotherapy of the Puerto Rico League against Cancer, Santurce, Puerto Rico

Carcinoma of the penis is the most common malignant tumor of this organ. It is said to represent from 1 to 3 per cent of all cancers in the male (McCrei, Ewing, Sibley, Paget, Billroth, Pack and LeFèvre, Von Winiwarter, Andrews, Wolbrust). In the Hospital of Oncology and Institute of Radiotherapy of the Puerto Rico League Against Cancer, in 4023 male admissions during the last 11 years, 145 cases (3.4 per cent) were carcinoma of the penis. Of these 124 were white, 21 Negroes. Thus there is not much difference in general or racial incidence in our series, nor in those reported heretofore.

In regard to age, the vast majority of cases occur between the ages of 40 and 70, though a considerable number are seen before 40 and quite a few after 70. Eight of our patients were under 30 when first symptoms appeared. The youngest was 22 years old on admission and symptoms had been present 1 year. We had two patients of 85 years. The average age for the whole series was 51½ years (table 1).

The cause of carcinoma of the penis, as of cancer anywhere else, is yet unknown. However, there are many antecedent circumstances which have been discussed as contributing factors. Of these, the most important is phimosis or a tight prepuce, which renders local hygiene difficult and retains secretions that give rise to prolonged irritation, which is the most serious predisposing cause (fig. 1 A).

A very high percentage of phimosis has been reported among cases of penile cancer (Barney 80-85 per cent, Dean 74 per cent, Demarquay 71 per cent, Förderl 89 per cent). In our series, it is specifically mentioned in 84 cases (58 per cent). In this connection, it is interesting to note that penile carcinoma is almost unknown in orthodox Jews, who practice ritualistic circumcision in early infancy. Circumcision later in life even in childhood does not give complete immunity. The fact that Mohammedans practice circumcision at 10, and sometimes develop cancer of the penis in adulthood, indicates that the precancerous changes can become well established at an early age and may progress to definite cancer formation even when the most important predisposing cause, namely phimosis, has been removed comparatively early in life (Dean).

Syphilitic and chancroidal lesions of the penis have been mentioned as causes of carcinoma (Patterson, Barney, Young, Demarquay, Förderl, Forster). In our series there is a definite history of chancre in 1 case, of antilucetic treatment in 16 and of positive serology in 22. Of the latter group we could confirm the positive findings in only 8 cases. It is most probable that antilucetic treatment was instituted in some of these cases without an established diagnosis of carcinoma. About the genitalia is not infrequently confused with the primary lesion of syphilis (fig. 1, B). It is well to remember that syphilis and carcinoma may co-

Read at annual meeting, Southeastern Section, American Urological Association, Memphis, Tenn., March 9, 1951.

2) It may grow toward the lumen in a bulky tumor mass, reducing the capacity of the bladder without, however, breaking through the mucosa. A reactive proliferation of the overlying epithelium may develop, thereby stimulating the development of fibro-epithelial sessile polyps. Although intimate relationship of tumor cells with blood vessels has been noted, active invasion and vascular dissemination are uncommon. The tumor infiltrates locally in the seminal vesicles, prostate, and rectum in the male. In the female, the uterus and adnexae may be involved. Local recurrence frequently appears in operative scars. Metastases have been reported in the skull, the skin, the pleura, the lungs, the intestinal mucosa, liver, heart muscle, regional and inguinal lymph nodes.

The treatment of choice is total cystectomy with inclusion of the entire urethra performed before extension to the surrounding tissues, distant metastases, severe infection or dilation of the upper urinary tract preclude it. Fulguration of the tumor seems to stimulate its growth and segmental resection has not proven satisfactory. Radiation is useful only as a palliative measure especially in the more rapidly growing tumors.

The prognosis of bladder sarcoma in children is poor. The mortality rate has been reported at 90 per cent for sarcoma of the bladder as a whole and 100 per cent for trigonal lesions. The average patient dies within 6 months after diagnosis. Survival of more than 1 year is unusual, although Hess's case of plexiform neurofibrosarcoma was living after 7 years with known residual tumor. Except for Feggetter's case, who was living and in apparent good health 12 years after excision and radiation, no authentic 5 year cures in children have been reported.

Two cases of sarcoma of the bladder in children have been observed by us.

CASE REPORTS

Case 1 (SGH No 140760) D. B., a white male, aged 10 months, was admitted to Spartanburg General Hospital on November 28, 1949. During the preceding 3 weeks the mother had noticed that the child was voiding frequently and in small amounts. There was associated straining, but no apparent pain. A lower abdominal mass which had not appreciably increased in size was noted 2 weeks prior to hospitalization. The child weighed 12 pounds at birth, and the only previous illness was pneumonia at 3 weeks of age.

Physical examination revealed a well developed and well nourished toxic infant who dribbled urine intermittently from the penis. A firm, irregular, tender mass the size of a grapefruit was present in the suprapubic region. The mass was slightly reduced in size, following catheterization, with removal of 8 ounces of clear urine. The skin of the penis and scrotum was slightly edematous and showed brown induration. Rectal examination showed the floor of the bladder indurated and the pelvic cavity filled with an irregular fixed mass which extended as far as the examining finger could reach.

Laboratory studies showed a mild anemia without leukocytosis, normal sedimentation rate and blood urea nitrogen 210 mg per cent with creatinine 9.8 mg per cent. The urine was sterile and contained 1 to 3 blood cells per high powered field. No renal function was demonstrated by excretory urography. A cystogram showed a large lobulated tumor mass involving the floor of the bladder, the distal

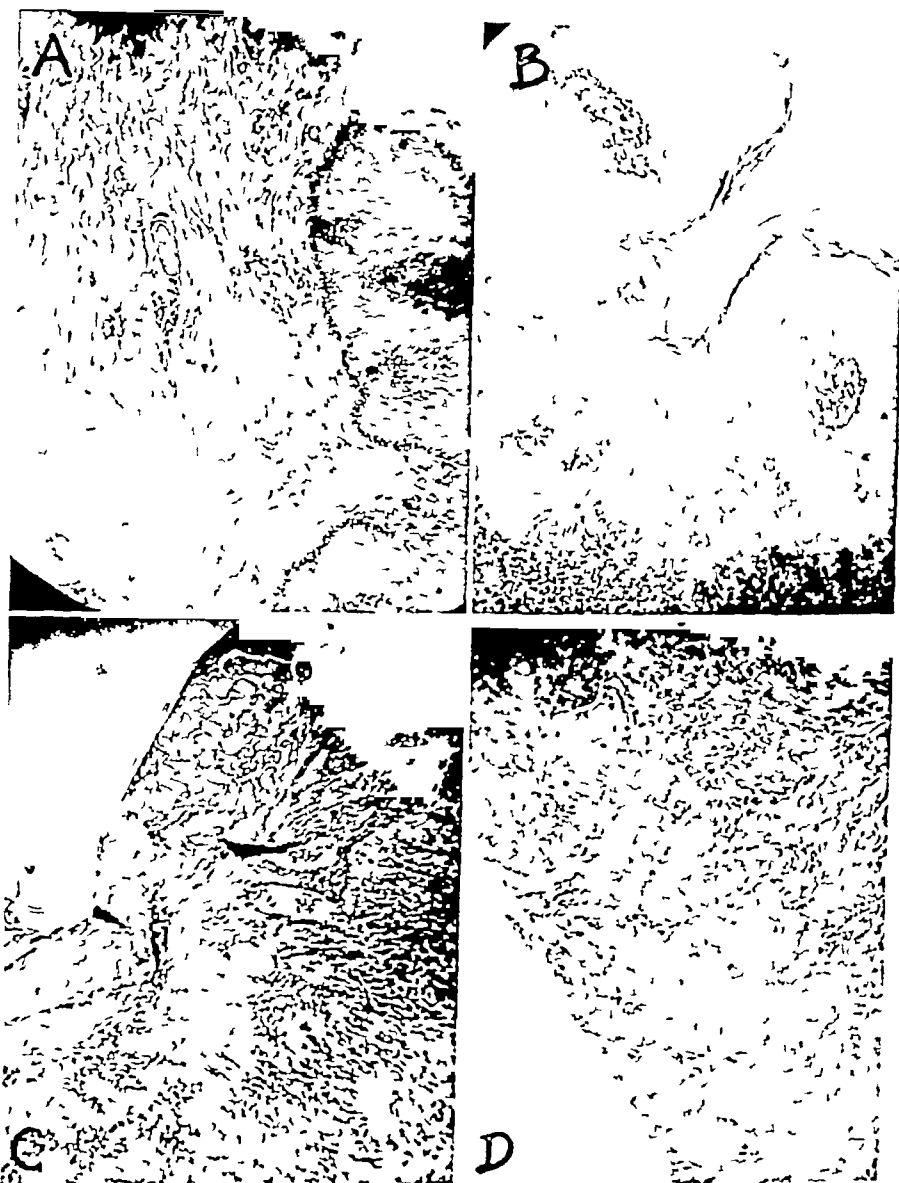


FIG. 2. A, acanthosis of lining epithelium within areolas adjoining patches of leukoplakia. Lesion appears to be in preleukoplakic stage. B, area of leukoplakia closer to tumor. Note intense inflammatory cell infiltration of subepithelial layer. C, step further advanced to B with acanthosis, parakeratosis and extensive hyperkeratosis. Changes upon basal cell layer are considerably advanced. Section is from tissue adjoining margins of growth. D, tumor showing typical epidermoid pattern.

a wart-like excrescence or a keratotic plaque. Ulceration occurs early and persists. In fact the commonest complaint is a sore which does not heal. This was so in most of our cases. In many instances the lesion hidden under a long foreskin, may be easily overlooked until it is far advanced. Attention is then drawn to it by the presence of a foul, irritating and sanguinous discharge.

bony pelvis and compressed the descending colon. The mucosal surface of the bladder was irregular. At the base there was a reactive proliferation with many edematous grapelike papillomatous masses which were especially prominent in the region of the trigone. The largest measured 3 by 3 cm.

Microscopic examination showed the bladder wall to be infiltrated with a spindle shaped cell tumor of fibroblastic origin (fig 3 A). The cells showed

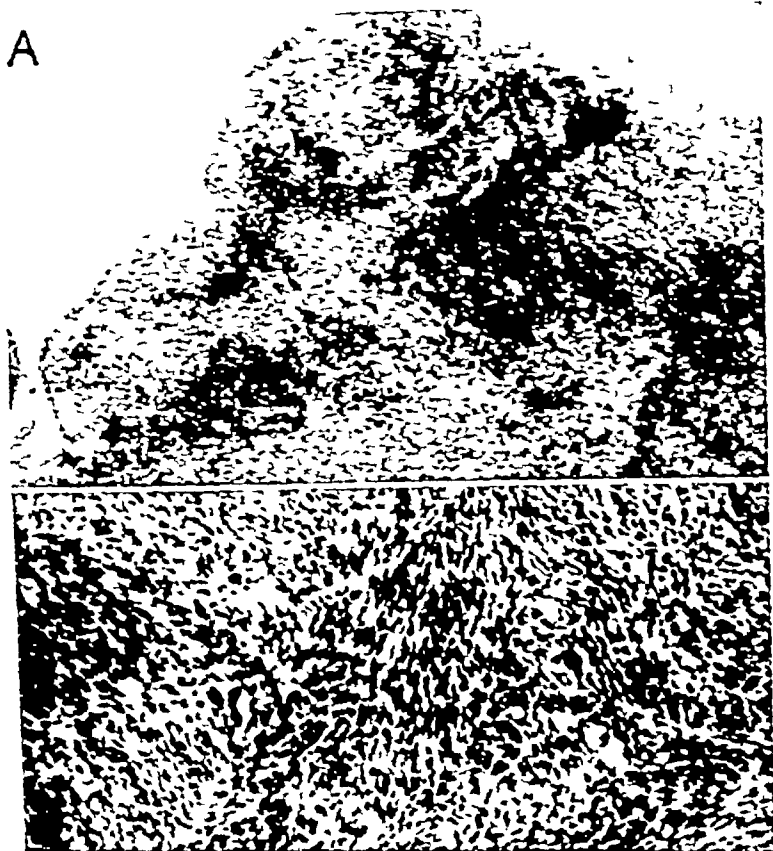


FIG. 3 A, case 1. Polypoid formation of bladder mucosa. Infiltration of bladder wall with spindle shaped cells of fibroblastic origin with irregularity of size, shape and staining reaction. B, case 2. Section through bladder wall showing characteristic spindle cells, which vary in size, shape and staining reaction.

irregularity of size, shape and staining reaction with occasional mitosis. In some areas mucosa had ulcerated with minor inflammatory reaction beneath. The intramural ureters were obscured by the tumor.

Case 2 (SGH No 2767) S. J. S., a white male, aged 2 years, was admitted to Spartanburg General Hospital on March 7, 1950. The mother stated that the child had been in good health until 3 weeks prior to admission, when he developed a chronic cough which resisted treatment. Two weeks prior to admission difficulty in voiding was noted without urinary frequency or apparent pain. For 2 to 3 days prior to hospitalization urination and defecation were accomplished after

the urethra and corpus spongiosum, which explains why in the most cases there may be pelvic metastases in the absence of inguinal involvement. Enlarged glands do not necessarily mean metastatic involvement. The enlargement may be solely due to inflammatory changes, which is specially true when the growth ulcerates and becomes infected. Then again nonpalpable glands may be the site of carcinomatous involvement. Lymph node involvement is usually bilateral but may be

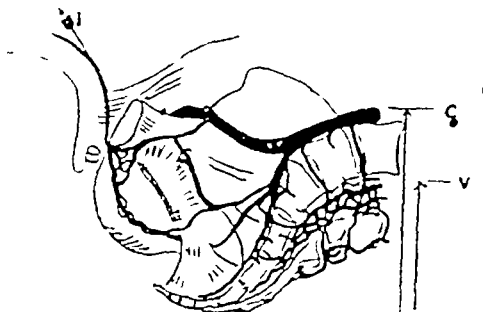


FIG. 4 Diagram of pelvic veins (lateral view). Shows pelvic anastomosis of deep dorsal vein of penis, *I*, *C*, vena cava, *V*, vertebral vein plexus. (From Batson, O. V. The role of the vertebral veins in metastatic processes. *Ann. Int. Med.*, 16: 38, 1942.)



FIG. 5 *A*, Hosp. No. 10879. Cancer of distal third of penis with inguinal adenopathy. Partial amputation with groin dissection. Pathological report: epithelioma; chronic lymphadenitis. Condition satisfactory 9 months later. *B*, Hosp. No. 9249. Cancer of penis with bilateral inguinal adenopathy. Partial amputation with groin dissection performed. Pathological report: squamous cell epithelioma; chronic lymphadenitis. Patient well after 21 months.

unilateral. In our series, 92 cases (63.5 per cent) had palpable inguinal adenopathy of which 50 cases (34 per cent) were metastatic.

Visceral metastases to the lungs, liver and bones generally occur late if at all. The diagnosis of penile cancer is made by biopsy. A dorsal slit may be necessary to expose the lesion. The disease is invariably fatal if left untreated. If it is seen early and there are no metastatic lymph nodes present, the prognosis is good if partial amputation is carried out 2 cm. proximal to any visible or palpable evidence of the tumor. The prognosis is grave if metastases are present.

Treatment varies according to the degree of involvement. Small growths in

Post-mortem examination showed numerous spherical, soft, yellow, metastatic masses scattered throughout both lungs. The largest measured 2 cm in diameter. There was a solitary mushroom shaped metastasis 2 cm in diameter involving the mucosa of the lesser curvature of the stomach (fig 4, A). The kidneys and ureters were normal. On the anterior surface of the bladder there was an ovoid, extremely soft, pale yellow tumor mass (fig 4, B) filling the prevesical space. The mucosal surface of the bladder was irregular, especially on its anterior aspect, but the tumor had not apparently extended through it. The posterior wall was not thickened and the trigone was not involved. The mass pressed the bladder, sigmoid colon, and rectum downward and backward, filling the entire hollow of the sacrum, which resulted in obstruction of the rectosigmoid colon.

Microscopic examination showed a spindle cell tumor of fibroblastic origin. The cells showed variation of size, shape, and staining reaction (fig 3, B). The tumor did not infiltrate through the entire wall of the bladder. It showed intimate relation of the tumor cells to the blood vessels accounting for the blood borne metastasis. Sections of the stomach showed metastatic tumor infiltrating from the outer wall to the muscularis mucosa and mushrooming the mucosa into the lumen of the stomach. The cellular characteristics of the gastric and pulmonary metastases were similar to the original tumor.

SUMMARY

Primary sarcoma of the bladder in children is uncommon. Ninety-one cases under 10 years of age were found in the literature. Two additional cases are reported. The tumor originates in the submucosal layer of the bladder, but seldom infiltrates through the mucosa. Distant metastases occur late. However, local invasion is more common and usually rapid. Cystography is more valuable than cystoscopy as a diagnostic aid. Total cystectomy with inclusion of the entire urethra offers the only hope of cure. Less radical surgery is not justified. Radiation is indicated only as an adjunct to surgery or as a palliative measure.

In the 2 cases reported, abdominal distention and difficult voiding were the predominate symptoms. Both, although far advanced, had sterile urine, normal except for an occasional red cell. The first case illustrates the effect of ureteral obstruction with resultant death from renal insufficiency. The tumor was thought to arise in the region of the trigone. In the second case the tumor originated in the anterior wall of the bladder, and the patient died as a result of multiple metastases.

Schuyler Office Bldg, Spartanburg, S C

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phylactic measure which should be always employed. The long prepuce in addition to predisposing to penile carcinoma conceals lesions which go undetected. With early circumcision, early detection and early adequate treatment, carcinoma of the penis can practically be eliminated from the death registry lists.

Radiotherapy alone, except possibly in small superficial lesions has proved unsatisfactory in the management of penile cancer and in the prevention or cure of inguinal metastases.

If the tumor is limited to the movable portions of the prepuce, its complete removal by circumcision gives satisfactory results, as illustrated by the 10 successful cases in this series, thus treated (table 2).

When the glans and distal end of the penis are involved, partial amputation with bilateral inguinal lymph nodes dissection gives the best curative results (table 2). Our personal experience does not justify the substitution of deep x-ray therapy for gland dissection in these cases.

The author wishes to express his recognition to Dr. Isaac Gonzalez Martínez, director of the Hospital of Oncology and Institute of Radiotherapy of the Puerto Rico League Against Cancer, to Drs. J. E. Taveras and I. Rivera Lugo, pathologists and Dr. H. Hazim, resident, who have all shared with him the study and care of these patients. Also to Miss Gloria Campos and to Mr. Federico Inzaray for their clerical help.

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THE BOLD EXCISION OF STRICTURES OF THE URETHRA WITH THE SMALL RESECTOSCOPE

EVERETT E. ANGLE AND LAVERNE F. PFEIFER

We wish to suggest a method of treatment for those urethral strictures that do not respond to usual dilatation with sounds. It is possible to excise the scar tissue with the loop of a resectoscope in rather a bold manner without running the risk of producing very much reaction. I say excise, and I do not mean incise. The scar tissue is removed some two-thirds of the way around the lumen or at least half way around the strictured area of the urethra. With these facts in mind the authors have used the resectoscope in recent years in treating a few strictures of the urethra.

The indications for the use of the resectoscope are: 1) It should be a stricture that has failed to respond to the usual method of gradual dilatation. 2) The stricture should be one that can be dilated to a point that a resectoscope can be passed and the strictured area visualized. 3) It should be a stricture of the pendulous urethra. 4) The patient should meet the same requirements as to the general physical condition, absence of infection, reasonable renal function, as for any other operation on the lower urinary tract.

A good way to select a suitable case is to do a cysto-urethroscopic examination with the McCarthy foroblique using the small sheath.

TECHNIQUE

Spinal or pentothal sodium anesthesia is used. Strictures are dilated by LeFort or other sounds until a junior type of resectoscope can be passed. It is the ideal instrument because the large resectoscope is too tight to manipulate. Once the instrument is passed, an assistant should keep the urethra straight by proper traction at the glans penis. The strictures usually run as bands around the lumen of the urethra, and stand out as white intrusions from the normal pink mucous membrane. They are carefully excised with a McCarthy resectoscope. It is rather important that the dorsal area of the urethra be the site of attack. Reasonable care must be taken not to cut too deeply if the ventral wall is to be attacked. The small resectoscope, which is of a caliber 16F, naturally can be passed by a smaller or more dense type of stricture and has such a marvelous lens system that the scarred area is well visualized. We do not recommend trying to pass a loop very far beyond the tip of the resectoscope. It is safer to use dilatation first so that the instrument can be passed beyond the scarred area and the entire resection done directly under vision. It may be necessary to pick up a few bleeding points and these should be coagulated with the least possible use of the diathermy current.

Our case reports are not numerous, but we wish to present one in detail because of the satisfactory outcome. Henry R. is a rural mail carrier. He has been in our office no less than 135 times. He was first seen in 1929, when 31 years of age. At that time he had fistulas in the perineum and a stricture of the pendulous

surgical specimen in cases which were not biopsied and where we did not suspect it, an experience which I am sure is not strange to most urologists. We then decided to include the following group:

C) A series of approximately 100 routine biopsies in an "all out" effort to see how many carcinomas we could detect by the biopsy method in patients who would be subjected to prostatic surgery, though the examiner on the basis of digital examination might not believe the gland to be malignant. Even if the gland was thought to be benign, a biopsy was taken from the most suspicious area in each case. The procedure was justified for the purpose of this study as we

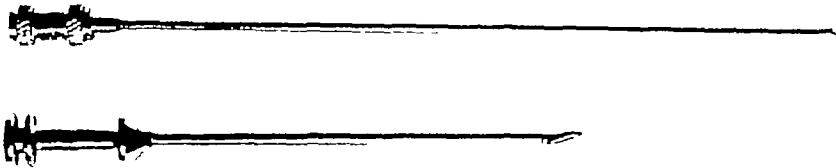


FIG 1 Turkel biopsy needle and prostatic biopsy specimen

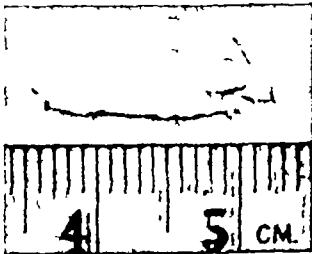


FIG 2

have found it to be harmless and we have seen no ill effects. These routine biopsies were usually taken at the same time and just before the prostetic surgery, thus causing the patient no additional pain or inconvenience.

	NO. OF CASES	CLINICAL IMPRESSION	BIOPSY	SURGICAL SPECIMEN
	84	Benign	Benign	Benign
	13	Malignant or ?	Benign	Benign (9 t u r)
	3	Benign	Malignant	
	34	Malignant	Malignant	
Six cases in which biopsy was wrong	2	Malignant	Benign	Malignant
	2	Malignant or ?	Benign	Malignant
	2	Benign	Benign	Malignant
	5	Malignant (one?)	Malignant	Benign (t u r)
	145			

DISCUSSION

In the total of 152 cases the biopsy was unsatisfactory 6 times, either it did not contain epithelial elements, or was unsatisfactory otherwise. Had we repeated these biopsies this figure might have been improved.

urethra that was calibrated to size 12. He was carefully dilated with bougies and got along reasonably well for several years. In 1937 he had a severe chill and fever following a dilatation, which was done with a filiform and LeFort sound. He was sent to the hospital and dilated under anesthesia to size 24, following which he had a few dilatations and three times in a row a retention catheter, size 14, was left in for 20 hours each time. This gave him some relief but through the years, 1937 to 1947, he was a frequent visitor at the office. The usual interval between treatments was 3 to 6 weeks. Shortly after the holidays in 1947 he was admitted to the hospital again. At this time he was 48 years old and gave the history of having had this trouble start with venereal disease at the age of 18. In other words he has suffered almost constantly from a small stream for some thirty years.

Inspection revealed a thin but well developed male, very apprehensive but in no acute distress. Physical examination was not remarkable. The prostate was small and normal in size, shape and consistency. By using the bougie a-boule, three strictures—two at the pendulous urethra and a larger more constricting one at the bulbomembranous junction, were found. Laboratory examination on admission showed that the urine was cloudy, specific gravity 1.025, albumin 2 plus, sugar 1 plus, hemoglobin 15 gm., white count 8,400. At operation, under pentothal sodium with curare, two bands of stricture in the pendulous urethra were resected endoscopically with the junior type resectoscope. A perineal incision was then used to expose the bulbomembranous urethra where another obstructing band was excised with the loop. A Foley catheter was introduced and the perineal wound was closed without drainage. The pathological diagnosis was fibrous inflammatory tissue from repair of the urethra. He received penicillin and stilbesterol for a few days. Catheter and sutures were removed on the eighth postoperative day followed by a chill and temperature of 104°F. The catheter was re-inserted and a large blood clot removed. The catheter was then removed on the following day. The patient was dismissed on the twelfth postoperative day voiding freely and easily. The postoperative course was uneventful. After 1 year the patient was voiding without difficulty. His last observation, now nearly 4 years later, finds him still voiding freely. A 24 sound passes with ease.

Table 1 gives the results in 6 cases. Only 1 case was a failure. We admit that the presence of an enlarged prostate or a bar makes it difficult to evaluate the result of excision of strictured areas.

In the last case edema developed immediately after resection of the stricture and the catheter was deposited through the sheath of the resectoscope before removing it.

Please do not undertake this procedure lightly. We have been bold in the amount of scar tissue excised but very timid in the selection of cases. We feel timid in presenting this procedure and recommend it only to the clergy in urology.

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palpation alone is relied on to make the diagnosis, as other conditions cause palpable changes in the prostate which simulate malignancy and further proof of diagnosis is indicated

CONCLUSION

Digital examination is the most valuable procedure for the detection of carcinoma of the prostate, but some malignancies will be missed, as 3.4 per cent were missed in this series of 145 cases. For a series of 100 routine examinations this figure is estimated at never 5 per cent. An error of 9 per cent was made in the group which were thought to be malignant or possibly malignant which were benign. For reasons already referred to this figure should probably be corrected to nearer 5 per cent in the routine digital examination of 100 cases. A total error of 12.4 per cent was made by digital examination and this might be corrected to 10 per cent. The error for the biopsy was 4.1 per cent for the series. Of the 56 cases which were thought on digital examination to be malignant or possibly malignant, 77 per cent were proven to be malignant and the biopsy verified or clarified the diagnosis in 95 per cent. In the 43 (77 per cent) proven cases the biopsy proved to be correct in 91 per cent. Since it appears that one can verify or clarify the diagnosis by such a simple procedure as a punch biopsy with from 91 per cent to 95 per cent accuracy in cases suspected of carcinoma on digital examination it would seem wise to use it even in the suspicious lesions. Verification of the malignant nature of the lesion before proceeding with treatment is important.

Surgical specimens from routine transurethral resection are not as reliable a check on malignancy as is ordinarily assumed, unless a special effort is made to get the characteristic tissue for diagnosis. If digital examination indicates the presence of a malignancy and examination of the surgical specimen (particularly when obtained by transurethral resection) does not demonstrate it, there is still a chance that a malignancy may be present. Further study by a perineal punch biopsy may be an easy way to prove it, as the specimen can be taken from the questionable area.

Drs D. E. Siler, A. D. Pipindra and Theodore Everett participated in the study as urological residents. We wish to thank Dr Edgar R. Pund of the Department of Pathology for his willing cooperation and Mr O. A. Parks of the Department of Art as Applied to Medicine for the illustrations.

Addendum. Since presentation of this paper, Hund and Sullivan (JAMA, 145: 1313, 1951) have reported the findings on rectal examination of 100 consecutive patients who subsequently underwent prostatic surgery. They found that 21 of these patients presented minimal suggestive signs of carcinoma. In 13 of these, the signs were attributed to associated nonmalignant disease and 8 were proven to have carcinoma when fixed sections were studied. It is of interest that their findings tend to parallel the findings on rectal examination in the above group of patients.

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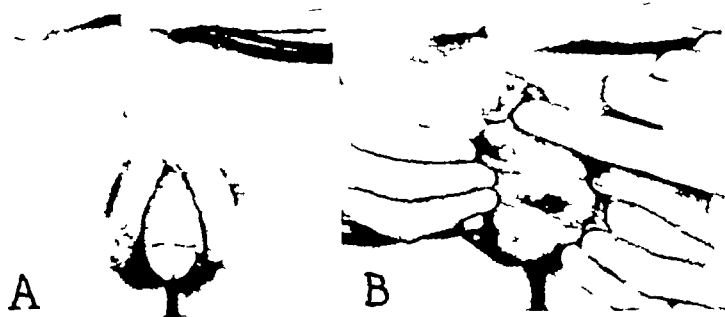


FIG 1 A, abnormal curvature of penis B, urethral orifice opening in scrotum

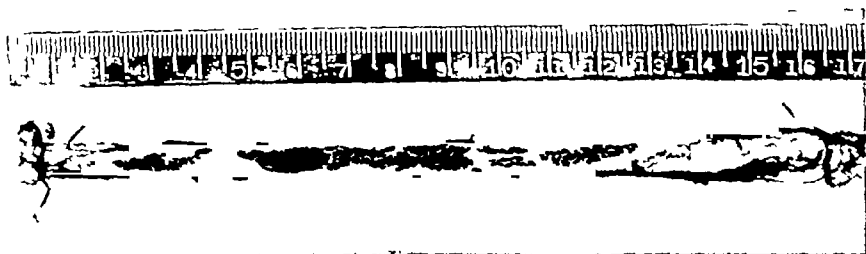


FIG 2 Urethra mounted on glass rod for preservation

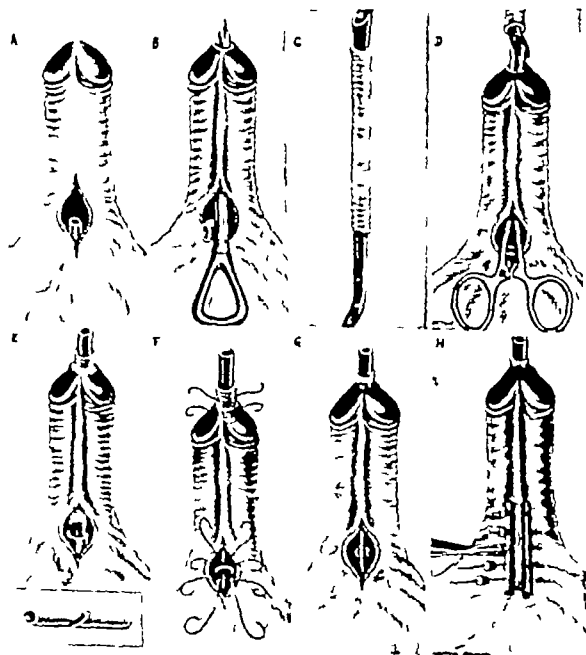


FIG 3

graft, that is, the new urethra, was then placed on a catheter, C, and passed through the tunnel (D and E) and sutured to the distal urethra and also to the skin penis by four No. 00 chromic catgut sutures (F and G). At the junction

postoperative course but was not seriously ill until his sudden death. Two deaths occurred more than one month postoperatively. One patient had a stormy postoperative course following a two-stage transurethral resection, never became ambulatory and eventually died of terminal pneumonia, senility and debility. The last patient died of pulmonary tuberculosis following a transurethral resection performed uneventfully while he was on that service.

There is a relationship between the length of time that a catheter is indwelling and the degree of postoperative fever. Accurate data showed that 78 patients undergoing transurethral resection had their catheter removed on or before the fourth postoperative day. A few patients had their catheter indwelling for a longer period. Eleven patients had a two-stage transurethral resection. An open prostatectomy was performed on 24 patients and all their catheters remained for more than four days. Those patients whose catheters were removed on or before the second postoperative day had a significantly less febrile course than those whose catheters were removed on the third or fourth postoperative day.

TABLE 1 *Comparison of risk to postoperative course*

	GOOD RISK PATIENTS	POOR RISK PATIENTS
	Patient under 46 and no serious complicating disease or operative complication	Patient over 45 or serious complicating disease or operative complication
Number of cases	47	82
Open operation	17%	19%
Transurethral resection	83%	81%
Average postoperative days	8	16
Death	0%	5%
Other serious complications	2%	7%
Afebrile postoperative course	23%	23%
Febrile more than one day	51%	57%

However, there was no significant difference in morbidity or mortality. Early removal of the catheter may reflect a technically better transurethral resection and more adequate hemostasis since the catheter was not removed unless the urine was clear or slightly tinged. These cases are not entirely controlled since the catheter was removed earlier more routinely by one resident. However, they include cases by other operators as well. It was the practice of some operators to remove the catheter earlier because of fever, so this factor may have tended to increase the febrile reactions in the early removal group. Those patients who underwent a two-stage transurethral resection, and of necessity had an initial technically unsatisfactory prostatectomy and longer period of catheterization had more febrile reactions, morbidity, mortality and postoperative period. The open operations were accompanied by a great number of febrile reactions and had a longer period of hospitalization, but there was no significant difference in serious complications or mortality. These findings are outlined in table 2.

At Franklin and the University of California Hospitals the postoperative clinical course of those who received chloromycetin did not differ significantly from those who received no prophylactic medication. Neither was there significant

The technique has given excellent results, at least just as good, if not better, than most of all the other procedures used in such cases

The risks are practically nonexistent because the infirmity of the patient cannot be worse after the operation than it was at the start

We believe that the formation of a fistula can be prevented by using a polyethylene or polyvinylite catheter instead of the ordinary catheter and thus avoid the tissue reaction at the point of junction. But we did not have that material in 1947

The procedure permits us to see great future possibilities, that is the creation of banks of urethras which can be utilized whenever needed, and this we are doing now

There might be a contraindication to this procedure on children because it is probable, though we have absolutely no proof of it, that the placing of such a graft may, due to the possibility of retraction of the tissue, stop the natural development of the penis, although this is still to be proven

Finally, to us, our results are convincing enough to say that the next time we have such a case, we will surely use this same procedure and we are actually preparing another case now for the same operation

ADDENDUM

Since this paper was prepared, two other patients have been operated upon by the same procedure with excellent results

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positive unless more than 50 colonies of bacteria per cubic centimeter of urine were present. Several negative cultures were obtained in the control series despite the presence of large numbers of bacteria in the stained smear. In both the control and chloromycetin series the preoperative cultures contained a wide variety of organisms and occasional mixed cultures. Following surgery both groups showed frequent changes in the bacterial flora of the urine, and mixed cultures often occurred. However, fewer patients receiving chloromycetin had urine

TABLE 4 *Preoperative and postoperative urine cultures*

	CONTROL SERIES		CHLOROMYCETIN SERIES	
Number of preoperative urine cultures	29		16	
Number of postoperative urine cultures	28		18	
TYPE OF BACTERIA	INCIDENCE		INCIDENCE	
	Pre op	Post op	Pre op	Post op
Negative culture and smear	5	0	3	0
Negative culture, positive smear	1	1	0	0
Staphylococcus albus	6	3	3	1
Staphylococcus aureus	1	2	1	1
Hemolytic streptococcus	2	3	0	0
Enterococcus	1	3	3	2
Coli	5	9	3	1
Aerogenes	5	10	3	2
Proteus	3	2	1	2
Pseudomonas	3	7	2	8
Alkaligenes	0	1	0	2
Mixed culture	2	12	3	1
Culture changed after surgery		18		7
Culture same after surgery		4		3

cultures containing the coli-aerogenes group of bacteria after surgery. These findings are summarized in table 4.

Twenty-seven patients received therapeutic drugs. Approximately half of these were from the control series. Many of these patients had fever without other signs and symptoms. Since many of the patients in this group recover in one or two days spontaneously or are aided by the removal of the catheter, the value of therapeutic drugs in this group is difficult to ascertain. However, in the more serious cases, a definite improvement could be demonstrated following the administration of the proper antibiotic. One of these cases is reported briefly.

CASE REPORT

J. E. entered the University of California Hospital on February 15, 1950 in acute retention. A diagnosis of a large carcinoma of the prostate with widespread

exist in the same lesion, also carcinoma and tuberculous penile ulcer. We had one of the latter extremely rare cases in our series.

Cases of epithelioma originating in circumcision wounds have been reported (Pitterson, Hermann, Young). In 7 of our cases there is history of nonhealing of circumcision wounds (fig. 1, C). It is possible that in these cases the cancer was already present at the time the circumcision was done (Young, Carbot).

Papillomatous vegetations, keratoses and leukoplakia are precursors of cancer (fig. 2). Many cases begin as a wart which may be malignant from the onset or

TABLE I. Carcinoma of the penis. Age incidence.

AGE (YRS.)	SCHREINER AND KRESZ	YOUNG BUT	VAEGELI UNIV. MINN. HOSPITAL	BARNEY MASS. GEN. HOSPITAL	DEAN MEMORIAL HOSPITAL	OUR SERIES PUERTO RICO
21-30	1	1	—	1	8	7
31-40	2	6	2	14	16	29
41-50	5	12	4	25	24	25
51-60	5	9	5	20	29	31
61-70	4	4	16	24	20	38
71-80	1	2	8	13	10	12
81-90	—	1	—	3	1	3
Total	18	35	35	100	108	145
Avg. Age	52.17	47.6	62.3	56.02	52	54.5

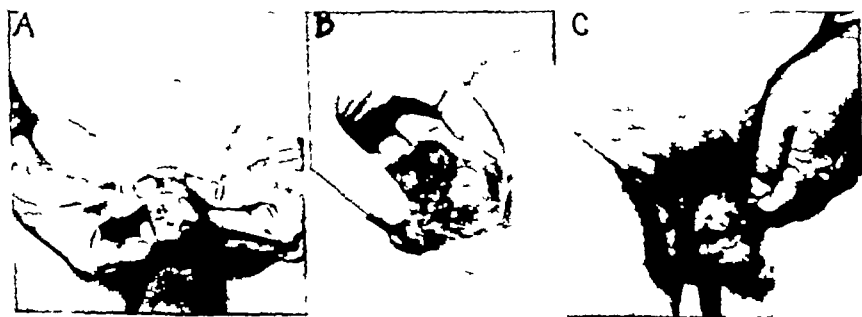


FIG. 1. A, epithelioma of glans penis hidden under phimotic prepuce. B, penile ulcer treated for lues before patient consulted us. Immediate biopsy revealed squamous cell epithelioma. C, nonhealing circumcision wound. Biopsy revealed epithelioma grade I (file p. No. 11545).

a benign wart (papilloma) which later may undergo malignant degeneration through chronic irritation (Himmelin, Ewing, Nelson, Young, Marshall). Most authorities agree that sexual intercourse with a woman having carcinoma of the cervix does not cause penile carcinoma.

Carcinoma of the penis is a lesion of the skin, definitely a skin carcinoma. Its very early lesions are not often seen because being relatively painless at first, the patient usually seeks medical advice at an unbelievably late stage of the disease. In our series the average duration of symptoms when first seen by us was over one year. The new growth may start as an indurated erosion or papule,

Hospital in 1948. High blood levels of penicillin and streptomycin at the time of operation or instrumentation in those patients with valvular heart disease may be of value to prevent an enterococcal septicemia or bacteremia. However, it has not been established by this series.

SUMMARY

The case histories of 129 consecutive patients who underwent prostatectomy were analyzed to determine what factors might influence the development of a febrile postoperative course.

The percentage of febrile reactions was similar in the good and poor risk groups, but the poor risk patients had more serious infections.

Early removal of the indwelling catheter reduces the incidence of postoperative fever following transurethral resection of the prostate.

Open operation is accompanied by a higher incidence of febrile reaction than transurethral resection, however, the incidence of serious complications is quite similar.

Chloromycetin, penicillin, and sulfadiazine used prophylactically did not alter the clinical postoperative course following prostatectomy.

The therapeutic use of antibiotics was extremely valuable in several cases.

CONCLUSIONS

Prophylaxis of urinary tract infection following prostatectomy depends primarily upon good, gentle, and aseptic technique with early removal of the urethral catheter.

The prophylactic value of the antibiotics has not been established, but may serve to alter the postoperative bacterial flora in the urine.

The therapeutic value of the antibiotics in those patients who develop serious reactions is well known.

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The most frequent site of involvement is the glans, coronal sulcus or the mucosa of the prepuce. The established disease assumes either the form of 1) a papillary excrescence or 2) an induration which is usually ulcerated. The first, commonly in the glans or mucosa of the prepuce continues to proliferate and when discovered appears as a papillary fungating, cauliflower-like foul-smelling mass. The second, usually in the coronal sulcus infiltrates and ulcerates deeply. As the malignant process progresses Buck's fascia and the cavernous bodies are invaded. The urethra and corpus spongiosum are rarely ever involved, we have never seen total urethral obstruction due to penile carcinoma. The ulcerative type metastasizes earlier than the fungating variety. Histologically, both types are squamous cell epithelioma or epidermoid carcinoma with pearl formation.



FIG. 3 Metastases to fourth lumbar vertebra from carcinoma of penis

and keratinization. In rare cases the cells resemble the basal cells of the epidermis and are called basal cell carcinoma. There is one of these in our series.

Extension of cancer of the penis occurs mainly through the lymphatics and the cavernous tissues. It does not send out long processes into the corpora. Like all other epithelial tumors it metastasizes by embolism. In one of our cases, there were metastases to the fourth lumbar vertebra (fig. 3) without evidence of local recurrence or inguinal lymph node involvement, which could only be explained by extension into the dorsal vein of the penis and spreading along the vertebral vein system as described by Professor Batson from Pennsylvania (fig. 4). Metastases may occur early especially in young patients but as a rule they occur rather late in the course of the disease whereas ulceration occurs early. Many patients have inguinal metastases when first seen. The common sites of secondary involvement are the superficial and deep inguinal lymph nodes and the nodes within the pelvis— all of which intercommunicate on each side and with those of the opposite side. Besides the pelvic nodes receive directly some of the lymphatics from

Twenty per cent of kidney wounds are associated with thoracic wounds (table 1)

The majority, 59 per cent of those tabulated in table 2, of kidney wounds are associated with wounds of other abdominal viscera. Collected statistics favor the conclusion that kidney wounds thus complicated have a graver prognosis than those in which the kidney alone is injured.

Recognition Recognition of kidney wounds requires examination for wounds of entry and exit with reference to the cross-sectional anatomy of the region. The presence of ecchymosis, of subcutaneous urinary extravasation, and of urinary drainage through open wounds must be noted.

TABLE 1 *U S Army, World War II Incidence of thoracic wounds with kidney wounds*

AUTHOR	NUMBER OF KIDNEY WOUNDS	NUMBER ASSOCIATED WITH THORACIC WOUNDS
Kimbrough	33	5
Marshall	24	9
Robinson et al	72	12
Total	129	26

TABLE 2 *British and U S Armies, World Wars I and II Incidence of abdominal visceral wounds with kidney wounds*

AUTHOR	ARMY	WAR	NUMBER OF KIDNEY WOUNDS	NUMBER OF ASSOCIATED WOUNDS OF ABDOMINAL VISCERA
Fullerton	Brit	I	53	35*
Imes	U S	II	41	29
Kimbrough	U S	II	33	11
Marshall	U S	II	24	13
Robinson et al	U S	II	72	52
Wallace	Brit	I	73	34
Total			296	174

* Figure includes cases with bone injuries

The urine must be examined for blood when renal injury is suspected in thoracic or abdominal wounds and the patient catheterized if necessary. Catheterization should not be done, however, until facilities for operation are available. Hematuria was found in 29 of 33 kidney wounds reported by Kimbrough and in 26 of 27 kidney injuries reported by Orkin. In 12 of Prather's 20 cases gross blood was present in the urine, and the rest showed microscopic hematuria. If the major renal injury is to the pedicle, or if the ureter is transected or obstructed by clots, hematuria may not be found.

X-ray examination of the kidneys when it is possible in the forward area is of great value. It should be done in all cases of suspected renal injury unless severe shock is present. If contrast media are not available, the flat film alone may be studied for clues to renal injury such as haziness of the renal outline, a hematoma mass in the kidney area, obliteration of the psoas outline, or the

the prepuce can usually be completely removed by circumcision. Small lesions, in some cases, have yielded to radiation. Larger lesions involving the glans and distal end of the shaft can be treated by partial amputation with removal of inguinal and femoral lymph nodes. If these nodes are badly infected or the patient is too debilitated, groin dissection can take place some days later. This will give the inflammation a chance to subside and also afford time to treat the patient with supportive measures and raise his resistance. If the patient's condition is satisfactory, the entire procedure, amputation with groin dissection can take

TABLE 2 Carcinoma of penis Results of treatment Hospital of Oncology and Institute of Radiotherapy Puerto Rico League Against Cancer Santurce Puerto Rico

TREATMENT	TOTAL	DEAD FROM OTHER CAUSE	LOST TO VIEW	1-11 MOS		1-2 YRS		2-3 YRS		3-4 YRS		4-5 YRS		6-10 YRS		TOTAL		PER CENT	
				A		A		A		A		A		A		A		A	
				D		D		D		D		D		D		D		D	
Radiotherapy (15)	9		2		3		3					1				1	6	14	85.7
\ ray only	2					1								1		2	0	100	0
Radium only	4				1	1						1		1		3	1	75	25
\ ray and radium (combined)																			
Local excision	5	1		4												4	0	100	0
Local excision & P O \ ray	7	1		1				1		2				2		6	0	100	0
Partial amp	20			5	5	1	3	1	1	1		1		2		12	3	80	20
Partial amp c \ ray	51	5		12	6	7	3	6	5		1	3		2	1	20	14	59	41
Partial amp c groin dis	9			1	4	1	3									7	1	87.5	12.5
Partial amp c groin dis & \ ray	20			3	3	3	2	1	3	2				3		13	4	76.5	23.5
Total amp c perineal urethrostomy and P O \ ray	3	1			1					1						1	1	50	50
Total emasculation c groin dis	1													1		0	1	0	100
Total emasc c groin dis & \ ray	2					2										0	2	0	100
Cases not treated for various reasons	12		0		5						1					0	6	0	100

* Palliative in 6 cases

puce in one sitting (fig. 5). Radical amputation with permanent perineal urethrostomy is done if there is extensive invasion of the body of the penis. Emasculation is considered unjustifiable in the absence of scrotal involvement.

The various forms of therapy employed in our cases and results obtained therefrom are summarized in table 2.

SUMMARY

We have presented a clinicopathologic study of 145 cases of penile carcinoma with a short review of the subject. This study reveals that the disease may appear at quite an early age and that phimosis is the most important predisposing factor.

Circumcision in early infancy (within the first two weeks) is an efficient pro-

years later, reported their successful use in the field in 4 cases. The patient was placed in the kidney position under endotracheal anesthesia. Resection of the tenth rib permitted exposure and repair of the lungs, kidney, and intraperitoneal viscera. The renal bed was drained when necessary and the diaphragm closed with separate layers of sutures to its pleural and peritoneal surfaces. The chest was closed in layers, aspirated immediately after operation and later when necessary. Marshall used this operation only on the left side. Chute, Soutter and Kerr have shown the value of the thoraco-abdominal approach for renal tumors on both sides of the body. The literature contains no reports of its successful use for war wounds involving the kidney and thorax on the right.

Once the kidney has been exposed what is done will depend on the type and extent of damage. Conservative primary surgery was possible in 151 of the 205 cases summarized in table 3. That this many kidneys could be saved is due in large part to the improvements in chemotherapy, blood replacement, and anesthesia which came into use during the course of the war. Data are not available

TABLE 3 *U. S. Army, World War II. Primary surgical treatment of kidney wounds*

AUTHOR	TOTAL NUMBER OF CASES	EXPLORATION DÉBRIDEMENT DRAINAGE OR PACKING	RENAL REPAIR	PRIMARY NEPHRECTOMY
Culp	43	25	8	10
Imes	36	16	4	16
Kimbrough	33	23	2	8
Marshall	9	2	5	2
Robinson et al	63	41	6	16
Total	205	126	25	54
Per cent of total		61	12	27

on the number of the tabulated cases which required late nephrectomy is the result of their wounds.

In all cases, débridement, exploration, and removal of foreign bodies is required. Perforating and penetrating wounds of the kidney without much disorganization may be treated simply by débridement, hemostasis, and drainage. Although packing may be used when necessary for hemostasis, it should be possible in most instances to control bleeding by properly placed sutures.

Lacerating wounds of the kidney should be treated by suture and repair. Even extensive lacerations of the kidney, provided the blood supply and kidney pelvis are intact, may not require nephrectomy. Figure-of-eight or mattress sutures are particularly useful in renal repair and hemostasis. Muscle high in content of thromboplastic substance, or fat, or the newer chemical hemostatic substances may be incorporated in these sutures for hemostatic purposes.

With the increasing experience now at hand in vascular anastomoses, suture of the renal vessels is possible and should certainly be tried, in suitable cases of wounds of the pedicle. The literature is yet without report of the successful employment of such methods in war casualties.

Nephrectomy, as primary treatment, should be reserved for cases showing

PERINEAL PUNCH BIOPSY OF THE PROSTATE WITH STATISTICAL ANALYSIS

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The following statistical study of 152 punch biopsies of the prostate was made in an attempt to determine the accuracy of this method of obtaining tissue for biopsy. The biopsy specimens were taken through the perineum with the Turkel biopsy punch (figs 1 and 2). It is not the purpose of this paper to discuss the various biopsy instruments, but we find this one to be satisfactory.

Data from both staff and private patients are included in this study. In each case, on the basis of digital examination, the examiner recorded his clinical impression as to the state of the prostate gland. Residents participated in the study so that the clinical impressions are not those of any one individual, nor was there always agreement. If the examiner did not have a firm opinion, but thought the gland was possibly or questionably malignant, it was recorded as such in order that the factor of guessing could be eliminated as much as possible. The biopsy in each case included in this study is proven to be malignant by pathological examination or in error by comparing the biopsy with the pathological report of the surgical specimen of the prostate subsequently removed by open surgery or transurethral resection.

GENERAL CONSIDERATIONS OF THE BIOPSY

1) The tissue removed must contain epithelial elements and be of sufficient size for the pathologist to make a satisfactory examination. With our present technique we have had little difficulty in fulfilling these requirements.

2) Tissue must be secured from the area which the examiner wishes and for this reason perineal biopsy is highly dependent on digital examination. Furthermore, this procedure should be considered an aid to verify the opinion gained by digital examination rather than the sole method of diagnosis. Obviously, a negative biopsy does not always rule out a carcinoma and there will always be a possibility of error. *This is an attempt to determine how often one can get an adequate biopsy of a definitely selected area and to establish the percentage of error.*

3) Criticism of the procedure is based on the theoretical grounds that it is possible to implant cancer cells in the tract of the needle resulting in carcinoma in the perineum. We do not know of any one who has seen this and we are unable to find a report of such a case in the literature. If any one has had such an experience they are remiss in not reporting it.

The clinical material consisted of

A) Cases which were thought to have carcinoma of the prostate clinically, and a biopsy was done to verify this opinion.

B) Cases in which a problem existed as to the nature of the lesion and the aid of the biopsy was welcome. Although we were checking these two clinical groups we were occasionally surprised that the pathologist reported a malignancy in a

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or nephrectomy. Conservation of renal tissue whenever possible should be the rule. Renal transplantation is undergoing experimental study at the present time and may prove to be of particular usefulness in some of these cases.

Persistent flank fistulas in some cases respond to simple ureteral catheter drainage. In others, secondary débridement, removal of foreign bodies, or secondary closure of fistulas may be required.

Cystic calcification of the hematoma after renal injury has been reported by Colston and Baker, and may require operation. Magoun has described a case of hydronephrosis due to ball-valve obstruction from a bullet lying free in the renal pelvis, for which nephrectomy was done. Hypertension has not been observed clinically as the result of renal injury.

Concussion injuries of the kidney. Concussion or blast injuries of the kidney have been described by Cannon and by Robinson and his associates. The cases reported by the latter group manifested renal pain and hematuria, with normal excretory urograms. All responded well to conservative treatment.

A group of cases of injury to thoracic and abdominal viscera due to underwater concussion was studied by McMullin and a group of Navy medical officers. Damage was confined principally to the hollow viscera and lungs. None of the immersion blast casualties were found to have kidney or bladder injury.

WOUNDS OF THE URETER

Occurrence. The ureters are deep, of small diameter, and related along their courses to the major abdominal viscera and spinal column. Wounds destructive enough to involve them are almost certain to involve other vital structures. Death is likely before the casualty reaches the forward hospital. Eighteen of the 25 ureteral wounds reported by Robinson, Culp, Suby, Reiser and Mullenix had injury of other abdominal viscera and 4 had fractures.

Recognition. Hematuria is diagnostic if injury to the kidney and bladder can be excluded and the ureter has not been completely divided or obstructed by clots. Likewise leakage of urine from the wound is a most important sign.

Excretory urograms should be made in all cases of suspected ureteral injury as soon as possible. They will often yield definite information on the extent and location of the ureteral wound, of the relative position of foreign bodies, and of the degree of associated skeletal damage. Excretory urograms in ureteral wounds may be done by the same methods, and are subject to the same limitations, as those for suspected kidney wounds. Retrograde examination, whether early or late, may be used when necessary and is even more accurate. The Briasch bulb-tipped ureteral catheter is of particular value in the production of ureterograms. Before exploratory operation, a ureteral catheter should be passed in cases of suspected ureteral injury when the patient's condition warrants.

Although laparotomy for abdominal wounds it is sometimes possible to recognize ureteral injury, the peril of unrecognized intraperitoneal urinary leakage from a damaged ureter is great and exact workup of cases of suspected ureteral wounds should be completed as early as possible.

One case was not classified as the patient had had a transurethral resection elsewhere a year previously and the specimen was reported to be carcinoma. He had been receiving stilbestrol and came to us for obstructive symptoms. The gland felt benign on digital examination, the biopsy was benign and the surgical specimen (transurethral prostatic resection) was benign. Although all of our tests were in agreement we believed that the stilbestrol had modified the microscopic picture.

Of the remaining 145 cases, 48 proved to be malignant by using all methods of study. In 42 of these the malignancy was evident in the biopsy while in 6 the biopsy was a false negative. In the group which were thought to be benign on digital examination 3 malignancies were discovered by biopsy. In 5 patients who were suspected of having a cancer from digital examination, the diagnosis would have been in error had we relied only on the pathological report of the surgical specimen obtained by transurethral resection. If we had relied on one method we would have discovered only 42 or 43 of the 48 cases as 5 were missed on digital examination, 6 on biopsy and 5 were known to be missed by transurethral resection so all of the methods had about the same percentage of error. This proved one assumption to be wrong in that we had originally assumed that the pathological report of the specimens obtained on routine transurethral resection would be a more reliable test of malignancy. This error in the transurethral resection group could no doubt be minimized if special attention were given to obtaining the specimen. Since the malignancy may be in the posterior lobe one could resect deeply using the palpating finger as a guide to the suspicious area. The separation of this specimen from the remainder of the tissue would no doubt be of additional help to the pathologist. It is also true that in enucleated hyperplastic adenoma might not contain any areas of malignant change and a malignancy could be present in the remaining portion of the prostate so the only absolute proof of benignancy would be the examination of surgical specimens obtained from total prostatectomy.

Of the 5 malignancies which were missed on digital examination, 3 were discovered by biopsy and 2 were not, a net gain of only 1 case where routine biopsies were taken without a suspicious area on palpation. Of 43 proven cancer cases which were suspected as malignant on digital examination, 39 were proven by biopsy. While the value of digital examination for the detection of prostatic cancer is well substantiated nonetheless some cases will be missed. Young has cited 25 cases in which the carcinoma of the prostate was missed, due to the absence of notable infiltration of the gland, and Ferguson's group C carcinomas are described as being regular in outline and rather elastic in consistency because of diffuse uniform invasion of the stroma. The error in calling a benign lesion malignant must also be considered and questionable lesions must be verified. We experienced the largest percentage of error in this group. Of the 56 cases diagnosed or suspected as being malignant in some degree on digital examination, 13 were benign and in all 13 the biopsy was benign. The "all out" effort to detect malignancy naturally weighted the study in this direction and 9 of the 13 cases were operated on by transurethral resection, another possible source of error in verification of the biopsy. In spite of these factors a real chance of error does exist if

anastomosis by pyelostomy or nephrostomy is required, to minimize extravasation. The classic technique of end to end anastomosis of the ureter consists of placement of fine, interrupted sutures outside the mucosa of the lumen. Robinson and his associates reported 3 cases treated by adaptations of this technique. In 2, good results were obtained but in 1 nephrectomy was required because of postoperative extravasation. Marshall reported 2 cases treated by end to end anastomosis. One was successful and one failed because of stricture.

Davalos, in 1947, reported experimental studies on a technique of ureteral anastomosis which yielded excellent results. This method, essentially an application of Gross's technique of arterial suture, consists of a continuous, extramucosal arterial silk mattress suture evecting the adventitial edges of the ureter. The development merits trial in suitable cases of war injury.

Lower ureter. Fifteen of the group of 25 war wounds of the ureter reported by Robinson and his associates involved its lower part. In some cases the methods described for treatment of wounds of the upper ureter are adaptable for the lower ureter. In others, particularly those with extensive damage of the lowest part of the ureter, ureterovesical anastomosis is required. Vaughan, as early as 1905, showed that this can be accomplished successfully after gunshot wounds. Robinson's group reported 2 cases in which ureterovesical anastomosis was undertaken as primary treatment. A perfect result was obtained in one. Graham and Imes have each reported cases treated early by this technique with good results.

It may occasionally be impossible at the first operation to find the end of the ureter or damage may be too great to permit anastomosis. Temporary nephrostomy, ureterostomy or flank drainage may be done pending later reconstructive surgery or, if necessary, primary nephrectomy carried out.

Complications and late surgery of ureteral wounds. In all cases of ureteral injury, whatever the treatment has been, prolonged observation for stricture is required using intravenous and when necessary retrograde pyelograms. Stricture, kinking or diverticulum formation from traction by scars may appear. These deformities may result in intractable urinary fistulas, hydronephrosis, pyelonephritis, lithiasis, or pyonephrosis if treatment has been unsuccessful.

At hospitals in base sections, ureteral strictures and fistulas may be studied accurately by excretory and retrograde urography, and by injection of sinuses with dyes. Late treatment may consist of catheter drainage, nephrostomy, end to end anastomosis, nephrectomy, or implantation of the ureter into bladder or bowel. The extensive scarring usually present makes good results more difficult to attain than would have been the case had primary repair been possible.

WOUNDS OF THE URINARY BLADDER

Occurrence. Bladder injury is common in wounds of the lower abdomen, hips, buttocks, thighs and perineum. Buttock wounds communicating with the bladder were found in 75 per cent of Fullerton's 53 cases and in 56 per cent of the 155 bladder wounds reported by Michels.

Associated wounds of the lower bowel appear to be the rule rather than the

EVALUATION OF FEBRILE RESPONSES FOLLOWING PROSTATECTOMY

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It has been shown that bacteremia frequently follows prostatectomy or urethral manipulation and causes febrile reactions of varying severity.^{1,2} Many factors may influence the development and severity of febrile reactions following prostatectomy, so these possible factors have been studied. The operative risk, type of operation, use of prophylactic medication and the length of time the catheter was left indwelling after surgery have been correlated to the degree of febrile response, morbidity, and mortality in 129 consecutive prostatectomies. Changes in the bacterial flora of patients' urine following prostatectomy were determined in those who received chloromycetin or no prophylactic medication. These patients were private cases of Drs. F. Hinman, D. Smith, J. Schulte, and F. Hinman Jr. at Franklin Hospital, clinic cases of the author at the University of California Hospital, and clinic patients of Dr. John Barr and the author at the San Francisco Hospital. All patients were operated between October 1949, and November 1950. Of the 47 consecutive cases from Franklin and the University of California Hospitals 24 received no prophylactic medication and 19 were given chloromycetin 1 gm. preoperatively and $\frac{1}{2}$ gm. daily during the postoperative period of catheterization. Two patients received sulfadiazine 2 gm. daily and two received 600,000 units of penicillin daily. Of the 82 consecutive cases at the San Francisco Hospital, 31 patients received no prophylactic medication, 20 received a combination of sulfadiazine 2 gm. and penicillin 600,000 units daily, 15 received sulfadiazine 2 gm. daily, and 7 received penicillin 600,000 units daily during the postoperative period. Nine patients received miscellaneous combinations of other drugs at the San Francisco Hospital. These cases either were receiving the other medication incidentally at the time of surgery or were selected as poor risk cases and so they are not included in the evaluation of prophylactic medication. The patients at the San Francisco Hospital were older, with fewer good risk patients than those at Franklin or the University Hospital.

The poor risk and good risk patients had a similar incidence of fever, but the former group contained all those who had serious septic reactions and had greater morbidity, mortality, and a longer postoperative period. These findings are outlined in table 1. Four hospital deaths occurred in the poor risk group. Two of these were in the immediate postoperative period. One was due to acute right heart failure after an otherwise uneventful recovery from the resection of a small median bar. He also had severe polycystic kidney disease and hypertensive heart disease. The other death was due to a cerebrovascular accident following a transurethral resection of a carcinoma of the prostate. This 76 year man had a febrile

¹ Scott W. W. J. Urol. 21: 527-566, 1929.

² Greavy C. D. and Feeney M. J. Bull. Univ. Minnesota Hospital & Minnesota Medical Foundation 20: 314-327, 1949.

reported a group of 155 cases treated in the forward area on this basis. In 119 the correct diagnosis was made preoperatively or at operation.

Notwithstanding that early exploration is usually required, other diagnostic methods are of tried value in the recognition of bladder wounds. First among these is catheterization with a soft rubber catheter and rectal examination with catheter in place. Catheterization should be withheld, however, until facilities for operation are available. Co-existing urethral wounds occur in a high proportion of bladder wounds and their detection by this means is important. Twelve urethral injuries were found in the 100 bladder wounds reported by Robinson's group. If the membranous or prostatic urethra is torn, the tip of the catheter hangs and may be located by rectal palpation. The examining finger detects infravesical extravasations of blood and urine as well. At the same time, extravasation is noted in perineum and scrotum. Successful placement of the catheter within the bladder demonstrates the presence or absence of urinary retention, while failure to obtain urine suggests intraperitoneal perforation.

X-rays of the pelvis in the field are necessary in a high proportion of cases for localization of foreign bodies and recognition of damage to the pelvis. If urethral injury is suspected, these films may be obtained with catheter in place. Retrograde cysto-urethrography with air or radiopaque media is a valuable aid in the diagnosis of bladder perforations due to nonpenetrating injuries, notably those associated with pelvic fractures. Its use in war wounds is generally considered unjustified.

A measured quantity of physiologic saline solution may be instilled through the catheter and withdrawn to determine if there has been loss of fluid from the bladder through a perforation. This has been recommended in cases of bladder perforation due to nonpenetrating injuries of the pelvis. The method is probably of limited value in war wounds.

Cystoscopy for diagnosis of bladder perforation in war wounds is not recommended. It contributes to shock in the unanesthetized wounded, it is technically unsatisfactory if intraperitoneal perforation exists, and it is less dependable as a means of diagnosis than is exploratory cystotomy.

Early definitive surgery. The principles of early surgical treatment of bladder wounds consist of cystotomy for hemostasis and repair of perforations, debridement and drainage of extravasations, and postoperative diversion of urine by suprapubic drainage. Intraperitoneal exploration and cystotomy are usually performed through the same lower abdominal incision. If the cystotomy incision for wounds of other viscera is inconveniently located, a separate suprapubic incision may be made for cystotomy. In some cases, exploration can be carried out by debriding and extending existing abdominal wounds. In others, new exploratory incisions are required.

The bladder is opened and explored. The ureters may be catheterized at this time to assure recognition of lower ureteral injuries. The edges of intraperitoneal perforations are excised to clean tissue. Intraperitoneal perforations are always sutured. Perforations in the base of the bladder located extraperitoneally are

difference in the postoperative course of those patients at the San Francisco Hospital who received penicillin and sulfadiazine alone or in combination prophylactically, or received no prophylactic medication. Neither the prophylactic

TABLE 2 Relationship of the type of operation and the duration of the indwelling catheter to postoperative clinical course

	TUR CATHETER INDWELLING 2 DAYS OR LESS	TUR CATHETER INDWELLING 3 TO 4 DAYS	TWO STAGE TUR	OPEN PROS- TATECTOMY*
Number of cases	37	41	11	24
Patient over 75	12%	27%	27%	33%
Carcinoma of prostate	16%	30%	27%	13%
Other diseases	69%	73%	63%	62%
Death postoperative	3%	5%	9%	0%
Serious postoperative complication	3%	3%	9%	4%
Average postoperative days	7	11	25	21
Afebrile (99.6 degrees or less)	49%	22%	18%	13%
Afebrile or febrile less than one day	80%	49%	36%	26%
Febrile 1-3 days	17%	39%	28%	53%
Febrile more than 4 days	3%	12%	44%	21%

* Open prostatectomy includes perineal, radical perineal, retropubic, and suprapubic prostatectomy.

TABLE 3 Relationship of prophylactic drugs to clinical postoperative course

DRUG	CHLOROMYCETIN	CONTROL	CONTROL	PENICILLIN AND SULFADIAZINE
Number of cases	19	24	31	46
Hospitals	Franklin and the University of California Hospitals		San Francisco Hospital	
Age over 75	5%	12%	29%	34%
Complicating disease	62%	88%	71%	78%
Open prostatectomy	21%	12%	10%	19%
Operative complication	0%	0%	3%	4%
Average postoperative days	7	7	14	16
Afebrile postoperative course	21%	25%	22%	26%
Febrile more than one day	42%	50%	48%	48%
Postoperative complica- tion	5%	8%	3%	4%
Postoperative death	0%	4%	3%	0%

use of chloromycetin, penicillin, nor sulfadiazine prevented the occurrence of epididymitis. These results are summarized in table 3.

Changes in the bacterial flora of patients following prostatectomy reflected the insignificant differences in the postoperative clinical course of those in the chloromycetin and control series. Cultures of the urine were taken prior to the institution of prophylactic therapy and surgery, and again 2 days after the catheter was removed. All the cultures were quantitative and were not considered as

5 months after a wound of the pelvis. In Lattimer's patient a fragment was recognized by x-ray near the bladder soon after the wound was incurred. No symptoms appeared until 8 weeks after injury when urgency, tenesmus and pyuria developed. The fragment, which had eroded into the bladder, was removed cystoscopically. Prather described a patient in whom dysuria and hematuria developed several weeks after sustaining shell fragment wounds of the buttocks and bowel. A shell splinter was removed from the trigone cystoscopically and a stone identified which was taken out through a suprapubic incision and found to contain another metallic fragment.

WOUNDS OF THE PROSTATE AND POSTERIOR URETHRA

Occurrence Wounds of the prostatic, membranous and bulbous urethra are usually associated with wounds of the abdomen, external genitalia, buttocks, thighs, perineum, bladder, rectum, or bony pelvis. Perforations of the bladder are not uncommonly associated with urethral injuries. This occurred in 3 of Poole-Wilson's 55 cases.

TABLE 5 *Civil experience. Incidence of vesical or urethral rupture in pelvic fractures due to nonpenetrating injury*

AUTHOR	NUMBER OF PELVIC FRACTURES	VESICAL OR URETHRAL RUPTURE	VESICAL RUPTURE	URETHRAL RUPTURE
Butt and Moore	126	16	5	11
Harrison	160	13	4	9
McCague and Semans	780	133		
Total	1066	162		

Fracture of the pelvis due to nonpenetrating injury was accompanied by rupture of the bladder or of the posterior urethra in 15 per cent of the 1066 cases summarized in table 5.

Recognition The principal signs of injury or rupture of the posterior urethra are bleeding at the meatus, or inability to void if the rupture is complete. Drainage from a local wound, if it occurs, is diagnostic. Diagnosis, when facilities for operation are available, is best accomplished by passage of a rubber catheter with rectal palpation of the urethra over it. Urine cannot be withdrawn though sometimes blood is obtained. X-rays of the pelvis with catheter in place yield necessary information on the condition of the bony pelvis and aid in localizing damage to the urethra. The rectal examining finger detects displacement of the catheter, displacement of the prostate, intravesical extravasations of blood and urine, and adjacent displaced fragments of the bony pelvis.

Extravasation of urine from the ruptured urethra into the tissues is commoner in small wounds than in large, open ones which afford free drainage. Culp has published a comprehensive anatomic and clinical study of urinary extravasations due to ruptured bladder and urethra. Extravasations in war wounds may not conform exactly to tissue planes because of disruption of the latter by missiles. In general, perforation of the membranous or prostatic urethra

metastasis and renal failure was made. The phenolsulfonphthalein output was 15 per cent in 2 hours, creatinine of 1.9 failed to improve on catheter drainage. On admission the urine was uninfected, but prior to surgery the urine culture revealed *Pseudomonas*. An incomplete transurethral resection of the prostate was performed under spinal anesthesia with minimal blood loss, and the patient remained in good condition in surgery and upon return to the ward. On the third postoperative day the patient had developed a septic temperature. A blood culture was taken, and dihydrostreptomycin 2 gm daily was started on the supposition that the fever was due to *Pseudomonas* septicemia. The catheter was removed. The patient voided poorly with stress incontinence. On the fourth postoperative day the fever progressed, and the patient appeared quite ill. The catheter was reinserted, dihydrostreptomycin discontinued. Polymyxin E 50 mg every 8 hours was started, still on the assumption that *Pseudomonas* was the infecting organism. On the fifth postoperative day the patient had a high fever and was comatose. His serum sodium was 116 meq and only a trace of phenolsulfonphthalein appeared in 2 hours. The blood culture was then reported positive for enterococci. A urine culture obtained on this day subsequently showed *Pseudomonas* 10,000,000 colonies per cubic centimeter and enterococci 500,000 colonies per cubic centimeter. Following correction of the sodium deficit, and therapy with aqueous penicillin of 4,800,000 units and dihydrostreptomycin 2 gm daily the patient survived. However, on discharge from the hospital, the urine still contained both organisms.

DISCUSSION

Creery has recently analysed 350 cases of transurethral resection and found that about half his cases had a fever of more than 101 degrees.² Approximately half of this series had an elevation of temperature that lasted more than 24 hours. He found that penicillin, sulfadiazine, and streptomycin alone and in combination did not lessen the incidence or severity of postoperative fever. Similar results were found in this series with respect to chloromycetin, penicillin, and sulfadiazine used alone or in combination. He also observed that poor risk patients and those who had excessive bleeding or operative complications were more likely to have serious septic reactions. His observation was confirmed by this series.

The most significant factor in reducing the incidence of postoperative fever was prompt removal of the urethral catheter, facilitated by a technically good resection and adequate hemostasis at surgery. Twenty-two years ago Scott recognized and stressed that many patients do not tolerate a catheter well and that a retention catheter should be removed when an unexplained fever occurs.¹ He also emphasized the importance of gentle aseptic technique and irrigation in the prevention of sepsis. These principles have not changed with the advent of antibiotic therapy.

Several cases of enterococcal endocarditis have been reported following instrumentation of the urinary tract.^{3,4} An unreported case occurred at San Francisco

¹ Menckly, J. K. Jr. *New Eng. J. Med.* 239: 708-709, 1948.

⁴ Merritt, W. A. *J. Urol.* 65: 100-107, 1951.

ary closure of open perineal wounds should be undertaken as soon as possible to minimize scarring and subsequent urethral deformity.

If, after perineal débridement, the edges of the urethra are accessible they should be sutured. If this is impossible, the more centrally located peri urethral soft tissues may be approximated over the catheter with expectation of recanalization. Colston reported 1 case, and Swersie 6 cases, of wounds of the bulbous urethra treated in the latter manner with favorable results.

When the urethra is completely severed and its ends can be mobilized and débrided, primary end to end anastomosis should be done over a catheter using fine, interrupted, chromic catgut sutures with as little tension as possible. The urethra is covered with as many layers of subcutaneous tissue as possible. War wounds treated successfully by this method have been reported by Michon, Stevens in the first war, and by Conger and Marshall in the second.

Operators familiar with the perineal approach to the prostate may elect to undertake primary repair of the ruptured urethra in the absence of open perineal wounds. The technique was originally described by Young for repair of ruptured urethra with fractured pelvis. Wounds should be drained to prevent localized infection and a 24 or 26F catheter fastened in the urethra as a splint. Secondary hemorrhage occasionally complicates urethral repair.

Perineal urethrostomy may be useful as a secondary procedure in wounds of the bulbous and anterior urethra if the suprapubic cystostomy fails to function well. Successful primary use of this type of drainage has been reported in several cases. Suprapubic cystostomy is to be preferred when evacuation of the case is anticipated through the hands of attendants unfamiliar with urologic procedures.

Identification of urethral fragments. Identification of the ends of the ruptured urethra may be difficult whether or not perineal exploration has been done. Several successful solutions to this problem have been reported. The coude rubber catheter can sometimes be gently introduced when it is impossible to pass a straight one.

A sound may be introduced through the penile urethra and another in retrograde manner through the cystostomy until the tips can be made to meet. The penile sound is then led into the bladder. G. G. Davis has recommended that the tip of the retrograde sound be ground hollow to engage the tip of the other. He used this device successfully in a case of ruptured posterior urethra without resorting to perineal exploration, and Poole-Wilson reported similar good results in 16 cases.

The sound, once introduced through the ruptured and displaced portions of the urethra, may be fitted tightly into the open end or the cut tip of a catheter and the catheter then drawn into place. If a small hole has been drilled through the tip of the sound a suture may be slipped through this and tied in the eye of the catheter.

Vermooten advises passage of a Foley catheter over a curved director through the penile urethra, using a finger in the prostatic urethra, introduced through the cystostomy, as a guide. The same maneuver may be used with a sound.

MANAGEMENT OF WOUNDS AND INJURIES OF GENITO-URINARY TRACT A REVIEW OF REPORTED EXPERIENCE IN WORLD WAR II

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The outbreak of fighting in Korea during the summer of 1950 has prompted us to undertake to collate and summarize the experience of surgeons treating urinary tract wounds during the second world war

The treatment of battle casualties may be regarded as having three phases 1) diagnosis and emergency management, 2) early definitive surgery, 3) later definitive surgery and management of complications These three phases of treatment are carried out at echelons in the rearward movement of casualties which vary with the tactical situation and depend upon theater evacuation policy Because the latter are the concerns of military command it is not our purpose to consider them in detail, but to confine our attention to aspects of the care of the wounded which are primarily matters of surgical judgement

The cardinal importance of antibiotics, of body fluid replacement, and of modern techniques in anesthesia in the successful management of war wounds was proved during the second world war Progress in these fields has continued so rapidly during the intervening 5 years that much of the wartime experience has been supplanted by more recent observations We have chosen therefore chiefly to consider the experience gained during and since the war in surgical technique

In genito-urinary tract wounds the objective of front line installations is the saving of life In forward surgical units urologic treatment is chiefly the emergency management of kidney and bladder wounds and the conservation of tissue in wounds of the external genitalia In addition however, it was shown during the last war that primary definitive treatment of ureteral and urethral wounds, when possible improves results strikingly and diminishes subsequent morbidity and disability materially

The management of urologic complications and secondary operative procedures for wounds of the urogenital organs can usually be undertaken in hospitals in the rear area where the necessary special equipment is available in the hands of experienced urological surgeons

For convenience in discussion wounds of the kidneys, ureters, bladder, prostate and urethra and the external genitalia are considered separately

KIDNEY WOUNDS

Occurrence Renal injury may be expected in 5 to 7 per cent of abdominal wounds and in about 10 per cent of thoraco-abdominal wounds

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retention occurring 3 years after gunshot wounds of the femur. A bullet was localized by palpation, x-ray and cystoscopy in the right lobe of the prostate and removed with the cystoscope. Pousson, in another case, removed a shell fragment from the prostate using the technique of perineal prostatectomy. This had caused a persistent urinary fistula 6 months after a buttock wound, and could be localized by palpation and by x-ray.

WOUNDS OF THE EXTERNAL GENITALIA AND ANTERIOR URETHRA

Early surgery. During initial treatment of wounds of the external genitalia, associated wounds of urethra, perineum, abdomen, thighs, and hips must not be overlooked. The principles of early surgical management consist of hemostasis and of débridement with conservation of all possible tissue. Every fragment of penile and scrotal tissue which might be of use in subsequent reconstruction must be saved. All testicular tissue with intact circulation should be preserved. Orchiectomy is reserved only for cases with complete loss of the blood supply to the testis.

Lacerating wounds of the testis should be débrided and the tunica albuginea repaired at the first operation. Drainage of scrotal wounds is usually unnecessary with present methods of chemotherapy provided hemostasis has been adequate. If the tunica albuginea is not closed at the first operation, subsequent infection results in swelling and herniation of the spermatogenic tissue and loss of the organ. Testicular wounds seen late, with well developed fungus of the spermatogenic tissue, should be operated on without delay. Meticulous débridement is done, sacrificing only enough normal tissue to permit closure of the tunica albuginea. Tissue about the upper pole is preserved as completely as possible to save spermatogenic function. The tunica albuginea is then closed. Fild better, at an Army general hospital, used this operation with good results in 12 cases. Ladwig, in the German army, used the same technique in a patient with only one remaining testis. Subsequent observation indicated intact spermatogenic function and normal libido.

In the presence of urethral injury an indwelling catheter is required to prevent urinary retention and to serve as a splint to prevent stenosis during healing.

In favorable cases, primary surgical repair of anterior urethral tears is possible. In a case reported by Campbell suture without tension was achieved by mobilization of the corpus cavernosum of the urethra. A good result was attained without use of an indwelling catheter.

Reconstructive surgery. Primary reconstructive surgery of war wounds of the external genitalia is possible in favorable cases reaching the advanced surgical hospital soon enough. Robinson, Stephenson and Padgett reported a case of partial transection of the penis with intact urethra. Eight hours after injury resuturing was done with good result. In another case, lacerations of the corpora cavernosa of penis and urethra were débrided and repaired 24 hours after injury. A promising result was apparent at 4 days. Secondary reconstruction of transected corpora cavernosa and bulbous urethra with good result was reported in 1 case by Poole-Wilson.

presence of a foreign body or free gas. When time or help is short or it is not desired to move the patient, the usual methods of excretory urography may be reduced to taking a single roentgenogram after dye injection. The majority of patients received are dehydrated and good dye concentration may be expected. Dye injection may be performed during early triage by a member of the shock team. A 15-minute film is then taken. If no dye excretion is apparent, another picture may be taken at 30 minutes. This film may be used to locate foreign bodies and studied for evidence of injury to the skeleton and abdominal viscera. The excretory urogram often permits accurate evaluation of the extent of kidney or ureteral damage. Its use is required to determine the presence of a normal kidney on the uninjured side. Eisendrath has computed the incidence of congenital solitary kidney at about 1 in 1000 individuals, and Turton and Williams have collected cases of traumatic rupture of a single kidney with fatal outcome because of failure to recognize the anomaly.

Urine and dye excretion may be suppressed in the injured kidney during the first 6 to 10 hours after injury. Urinary suppression occasionally may occur in both kidneys, Orkin reported this phenomenon in 2 of his 27 cases.

Cystoscopy and retrograde pyelography are valuable supplements in the diagnosis of renal injury but in the field are of limited usefulness and should only be undertaken by experienced operators. These procedures are hazardous in the presence of shock or of extensive pelvic fractures. Nevertheless, they yield definite, accurate information on the condition of both kidneys and the risk of infection resulting from cystoscopy is slight.

Early definitive surgery. Except in occasional cases with massive hemorrhage, surgical intervention should be delayed until shock has been controlled. Laparotomy is indicated when combined wounds of kidney and of the abdominal viscera are suspected. In such cases, renal and retroperitoneal exploration are required. In the majority of cases of this type reported by Robinson, Culp, Suby, Reiser, and Mullenix and by Prather, renal injury was recognized because of retroperitoneal hematoma noted at laparotomy.

When delay in making an additional incision is not warranted for treatment of the kidney injury, the kidney may be approached transperitoneally. This operation is more difficult on the right than on the left. It may occasionally be desirable to close the peritoneum after abdominal exploration, extend the incision laterally, and proceed with retroperitoneal exploration.

When the extraperitoneal flank incision is used, this may be made by debriding and extending one of the existing wounds, or a large, new, well placed incision may be made to assure best possible exposure of the kidney. The flank incision may be of the classic, oblique, subcostal type, or transverse. Both types of incision may be extended anteriorly to permit exploration of the upper abdominal cavity. The twelfth rib may be resected to give wider exposure. This is of particular advantage in the presence of extensive kidney damage, large hematoma formation or obliteration of normal landmarks.

Fullerton in 1922 suggested combined thoraco-abdominal incisions for kidney wounds with associated intrapleural and intraperitoneal injuries. Marshall, 24

The great majority of bladder perforations due to war injury are intraperitoneal, and wounds of the small or large intestine or rectum are usually found. Early exploratory laparotomy and cystostomy is mandatory in most cases. Intraperitoneal and accessible extraperitoneal perforations are sutured. Perivesical and prevesical spaces are débrided and drained. A urethral catheter is left in place if urethral wounds are present. Postoperative urinary drainage is assured by placing a large suprapubic tube high in the bladder.

In wounds of the prostatic, membranous and bulbous urethra prompt diversion of urine by cystostomy and drainage of extravasations is required. Restoration of urethral continuity is best accomplished at the time of the first operation before scarring and deformity have occurred. A urethral splinting catheter is left in place. In some cases suprapubic technique for approximating the torn ends of the urethra can be used. When open perineal wounds exist and in certain other cases, repair of the urethra can be accomplished perineally. Early secondary closure of open perineal wounds is necessary to minimize scarring.

Early treatment of wounds of the external genitalia consists of hemostasis and conservative débridement. Testicular lacerations, seen early or late, should be débrided and the tunica albuginea closed to prevent herniation and loss of spermatogenic tissue. The testis is preserved in all cases unless its blood supply is destroyed. Anterior urethral injury necessitates use of an indwelling urethral catheter, and repair if tears are present. Reconstruction of damaged corpora cavernosa of penis or urethra should be attempted as early as possible. Plastic surgical procedures for replacement of skin loss from penis and scrotum may be done primarily in favorable cases or delayed until a clean wound has been obtained.

SUMMARY

Published experience of surgeons treating wounds of the urogenital organs during the second world war has been reviewed, collated and summarized with reference to recent advances in surgical technique.

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continued massive hematuria, uncontrollable hemorrhage or urinary extravasation, or in which operation has revealed massive destruction or infarction of renal tissue Parker concluded from British experience that a rising pulse rate is the most reliable indication of progressive hemorrhage in these cases

Nephrectomy is required for secondary hemorrhage whether it occurs after open wounds or nonpenetrating injuries of the kidney. This grave but comparatively infrequent complication may be expected during the second and third weeks after injury. It occurred in 2 of the 27 cases of nonpenetrating injury reported by Orkin. Bed rest for at least 10 to 14 days after injury is required as a prophylactic measure.

Nephrectomy is indicated in certain cases of overwhelming infection.

Nonpenetrating kidney injuries. A large and excellent literature has developed in recent years concerned with nonpenetrating injuries of the kidney seen in civil practice. Because of the increasingly wide use of motorized and armored transport in modern war it may be expected that this type of injury will occasionally be encountered in the field.

In most cases injury is due either to impact of the kidney on the twelfth rib or of the rib upon the kidney, depending on direction of the blow. All degrees of damage to the kidney, pelvis and pedicle may occur, from contusion and laceration to extensive rupture and infarction. The typical clinical picture consists of flank pain and hematuria, shock, reflex gastro-intestinal disturbances and often a flank mass due to extravasated urine or blood. Excretory urograms should be made but their usefulness may be impaired by unsatisfactory definition of the extent of renal damage or by reflex anuria. It is in such cases that retrograde examination should be performed.

The most important radiographic signs include hematoma shadow in the kidney area, obliteration of the psoas outline, extravasation of dye, and distortion or displacement of pelvic or calyceal shadows. The presence of a normal kidney on the other side must be determined before operation.

Conservative treatment has been possible in the majority of cases. Operation is indicated by increasing flank tumor, continuing massive hematuria or urographic evidence of severe renal damage. At operation, as in open wounds, hemostasis or repair may often be accomplished without nephrectomy. The indications for nephrectomy parallel those in open kidney wounds: uncontrollable hemorrhage or urinary extravasation, massive destruction or infarction of the kidney or secondary hemorrhage.

Late surgery and the management of complications. In all cases of renal injury, whether due to penetrating wounds or indirect violence, periodic urine examinations and intravenous urograms are necessary after apparent clinical recovery. Patients with a history of wounds or injuries of the mid-trunk with late symptoms referred to that area merit complete urologic study.

Deformity of renal substance or distortion of the calyces, pelvis or ureter due to scarring may develop and interfere with urinary drainage. Strictures, persistent fistulas, intractable urinary tract infection, calculus formation, pyelonephrosis or hydronephrosis may appear, any one of which may require repair.

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Extraperitoneal urinary drainage from a damaged ureter appears to be less dangerous to life than from the kidney, bladder or urethra. Urinary extravasation in the flank, even without drainage, appears to be reasonably well tolerated.

Primary recognition of ureteral wounds in the last war was uncommon, having been possible in only 7 of the 25 cases reported by Robinson's group. Urinary fistulas in the unrecognized cases developed from 7 to 10 days after injury. If tissue has obstructed the wound tract, retroperitoneal extravasation produces a flank mass which usually becomes infected.

Early repair of ureteral wounds. In war wounds of the ureter and urethra alike, best results are obtained by early re-establishment of continuity of the channel over a catheter with diversion of the urinary flow above the injury. Local urinary extravasation and infection are minimized. Scarring is less dense. Stricture formation, ureteral deformities and interference with drainage are less frequent and when they occur are more readily managed with sounds.

Upper ureteral wounds. The technique chosen for re-establishing ureteral continuity must be adapted to the location and extent of damage in each case. Rarely a ureteral wound will heal and the fistula close spontaneously without stricture formation. Everidge and Barnes and also Prather have each reported such a case. Successful results have also been obtained merely by placement of an indwelling ureteral catheter. Heitz-Boyer, in the French army in the first world war reported a case in which a loin fistula seen on the sixth day after injury healed over a catheter left in place for ten days. Culp reported 3 similar cases in which healing occurred over catheters left in place for 3, 4 and 7 days.

Generally, if the patient's condition permits, early operative repair of the ureter should be undertaken. In all such cases diversion of the urinary stream above the injury by pyelostomy or nephrostomy is necessary. Any standard catheter of suitable type may be used for this purpose. The smaller, ureteral splinting catheter should also be brought out through the renal pelvis or parenchyma. Extraperitoneal soft tissue drainage is usually required.

If sufficient ureteral wall remains a longitudinal laceration may be treated by simple suture, leaving a splinting catheter in place. Everidge and Barnes reported a case treated this way with a good result.

During and since the war D. M. Davis and his associates have reported on the technique of intubated ureterotomy. This method should prove to be well adapted for use in war wounds with loss of a longitudinal segment of the ureteral wall. The principle consists in placing a long 12 or 14F soft rubber splinting catheter within the damaged ureter. Pyelotomy is performed, and the catheter left in place for 4 to 6 weeks. Experimental studies have shown that regeneration of the mucosa and muscularis is complete within this period. Catheters of synthetic plastic materials have recently been found to cause a minimum of tissue reaction and encrustation and should be used if they are obtainable.

Davis's technique may also prove useful in the management of ureteral strictures appearing as the late result of war injuries.

Transverse injuries of the ureter require debridement of the injured ends, careful suturing and a splinting catheter. Diversion of the urine above the

EXFOLIATIVE CYTOLOGY OF TRANSITIONAL CELL CARCINOMA

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Experience with abnormal cytology occurring in the urinary sediments of renal parenchymal malignancies has been reported.¹ This has been promising but far from satisfactory on the basis of present morphologic criteria. However, transitional cell carcinoma material has been very satisfying and reliable as a diagnostic clinical aid.

Abnormal and normal cells are detected in the urinary sediments stained by the Papanicolaou method, by morphologic differences. These are briefly: reduction in the nuclear-cytoplasmic ratio, thickening of the nuclear membrane, granular, prominent chromatin network, bizarre, irregular and often multiple nucleoli, etc. The "tadpole" cell, so named because of its resemblance to a tadpole, has suggested transitional cell carcinoma.

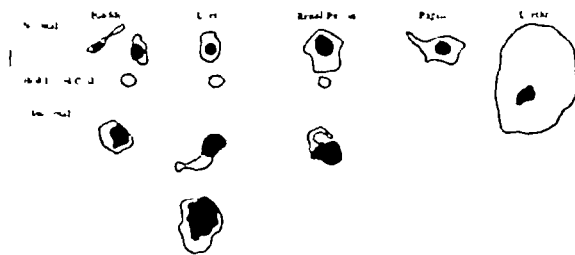


FIG. 1 Camera lucida drawings, normal and abnormal cells

Camera lucida drawings (fig. 1) made at 500 diameters' magnification give a scale of comparison with normal cells and red blood cells. The size of the cell has little morphologic significance to the detection problem, and nuclear changes are of the maximum importance.

In order to eliminate possible errors arising from hyperplastic and regenerating epithelial cells, observations were made on cells exfoliated from a piece of granulation occurring in the ureter, from metaplastic growths in the pelvis of the kidney, as observed through the cystoscope in a nephrostomy wound, and those present in the urine following transurethral prostatic resections.

Figures 2, 3, 4, 5, 6, 7, 8 and 9, with their legends, are illustrative of my material.*

In vitro cultivation of one of the tumors was made (I, II) both in routine and synthetic media.² Cells growing in the tissue culture often assumed the "tadpole" shape especially when they were floating free in the medium and resembled morphologically the exfoliated forms in the urine.

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* Bunge, R. G. and Kraushaar, O. F. J. Urol. 63: 175, 1950.

Another was described and illustrated in a previous article. Bunge and Kraushaar. Abnormal Renal Cytology. J. Urol. 63: 173, 1950.

² Bunge, R. G. and Stein, R. J. J. Urol. 64: 646, 1950.

exception. In 70 per cent of the 315 bladder wounds on which data could be obtained (table 4) wounds of the small or large intestine, or of the rectum, were present. Purely extraperitoneal wounds are uncommon. Eighty-three per cent of the 262 cases summarized in table 4 had intraperitoneal or combined intraperitoneal and extraperitoneal perforations. Prognosis is poorer when intraperitoneal perforations are present. Injury to the bony pelvis is common. It occurred in 25 of the 100 cases summarized in the report by Robinson, Culp, Suby, Reiser and Mullenix.

Recognition. Early recognition and treatment of wounds of the bladder and posterior urethra are of prime importance. Unrecognized or untreated urinary extravasations, with infection, in the peritoneal space or in the retroperitoneal or perivesical tissues carry a high mortality.

The symptoms of bladder perforation are hematuria, prevesical pain, vesical tenderness, or inability to void. Hematuria is present in most cases. It was reported in 150 of Michels' 155 cases. The other symptoms are of relatively little

TABLE 4. *British and U. S. Armies, World Wars I and II. Incidence with bladder wounds of intraperitoneal perforation and bowel wounds*

AUTHOR	ARMY	WAR	NUMBER OF BLADDER WOUNDS	INTRAPERITONEAL OR COMBINED INTRA- PERITONEAL AND EXTRAPERITONEAL PERFORATIONS	ASSOCIATED BOWEL WOUNDS
Fullerton	Brit	I	53		35*
Marshall	U. S.	II	7	5	5
Michels	U. S.	II	155	137	134
Robinson et al.	U. S.	II	100	70	61

* Figure includes cases with bone injuries.

clinical importance, often masked by shock and the multiplicity of accompanying injuries.

In all cases, examination of the patient for wounds of entry and exit with reference to the cross-sectional anatomy of the region is required. In some cases, suprapubic urinary extravasations may be found. The abdomen should be palpated for bladder distension.

Urinary drainage from a wound in the region of the pelvis is diagnostic of perforation of the bladder or lower ureter. Urinary drainage from the rectum, or passage of feces in the urine, indicates rectovesical perforation.

Because of the high frequency of intraperitoneal vesical perforations and of associated bowel injury, most cases require laparotomy. The high mortality of unrecognized urinary extravasation and peritonitis or retroperitoneal and perivesical cellulitis makes exploratory cystotomy mandatory at the first operation in nearly all cases. Kimbrough, summarizing American experience in the European theater, emphasized the necessity of making the diagnosis at the time of first examination and primary operation. Lewis's recommendation is quoted:

When in doubt it is safest to explore and drain the bladder. The scalpel is the best emergency instrument. Wallace, reviewing British experience in the first war, concluded: 'It is safer to look and see than to wait and see.' Michels



FIG 4 L. T., a white man aged 70, complained of hematuria of 24 hours' duration observed to be coming from left ureteral orifice. *A*, filling defect in ureterogram and gross specimen; *B*, cells collected from left ureter; *C*, microscopic section of tumor.



FIG 5 J. H., a white man aged 64, had intermittent hematuria for 2 months. Left ureterogram with filling defect in lower one-third, and gross specimen.

In 1895 Rovsing³ stated that early diagnosis of renal cancer was possible by detection of tumor cells in the urine. In three out of seven cases, the urinary

³ Rovsing, T. Arch. i. klin. Chir. 49: 40, 1895.

repaired when this is technically feasible. Failure to close the bladder, in the presence of adequate drainage, appears to be of secondary importance though convalescence may be prolonged.

Repair of perforations is carried out using interrupted sutures of catgut extramucosally. If hemostasis is required, sutures may include the full thickness of the bladder. The perivesical and prevesical spaces are debrided and drained through separate incisions if necessary. The consensus is that the prevesical space should usually be drained, though opinion differs on the desirability of this as a routine procedure. If there is co-existing injury of the urethra, an indwelling catheter is placed. Peritoneal drainage, though widely favored during the first war is unnecessary with contemporary chemotherapeutic methods. A large (34F) suprapubic tube of the Malecot or Pezzar type is placed high in the dome of the bladder. High position of the tube is necessary to protect the trigone and symphysis. The catheter is brought out along an oblique tract to facilitate subsequent healing.

The majority of observers during the second world war agreed that suprapubic drainage is the safest and most dependable type after repair of bladder perforation. It is particularly necessary when casualties may be evacuated to the rear without assurance of sustained and careful attention to their catheters. Successful use only of an indwelling urethral catheter for postoperative drainage has occasionally been reported. Robinson and his associates described 5 cases of bladder wounds in which urethral drainage alone was used after repair. In 4 of these cutaneous urinary fistulas developed through the wounds of entry or exit.

When rectovesical perforation exists, colostomy as well as cystotomy is required.

Blast injury of the bladder. Culp described 4 patients who had frequency, urgency and hematuria after being in the vicinity of explosions. All had microscopic hematuria and showed punctate hemorrhages by cystoscopy.

Late surgery and complications. Robinson and his colleagues, reporting on 100 cases of bladder wounds of which 81 were treated by early suprapubic cystotomy, observed the following late complications: 15 cutaneous fistulas other than suprapubic, 1 perivesical abscess and 2 cases of pyelonephritis. There was 1 death from urinary peritonitis.

Hawes found that late cystographic observation of patients with bladder wounds may show deformities due to displacement by bone fragments, hematoma or traction due to adhesions. Bladder calculi may be observed in patients with strictures or fractured pelvis.

After cystotomy and colostomy MacLachlan observed that many rectovesical fistulas closed spontaneously. Standard operations for rectovesical fistula should be possible should spontaneous closure fail to occur but no reports could be found relative to this problem in war wounds.

After wounds of the lower trunk or thighs without suspected bladder injury, metallic fragments may occasionally migrate into the bladder and cause late urinary symptoms. Bors and Bowie reported a case in which hematuria appeared

sediments contained tumor cells. Ten years later Albrecht⁴ investigated the urinary sediments in 23 cases of parenchymal renal tumors and was disappointed in the results. Shainoff and Sala, seeking to explain vaginal metastases from "hypernephroma," failed to find tumor cells in the urine.⁵ However, cytologic examination of the urinary sediment can be and has been a useful clinical aid to the urologist. It will confirm the impression gained from x-ray studies and will aid in differentiating nonopaque stones and blood clots from tumors and prevent delay in diagnosis. In equivocal x-ray studies, it will dictate further in-



FIG. 9. Case of H. P., a white man, aged 77. *A*, air cystogram showing bladder tumor; *B*, cells from bladder urine.

vestigation. To surgeons who are doubtful of its value, it will, at least, warn them to be prepared to perform a complete unilateral extirpation of the upper urinary tract if the preoperative impression is erroneous. Further aid may be obtained in certain cases where it is impossible to determine cystoscopically whether inflammation or infection with neoplasms exists. Biopsies may be misleading from failure to select a proper site. Bladder cytology will mirror the entire bladder.

Another useful aid has been in postoperative bladder fistulas. The presence of residual neoplasm as indicated by the cytology of the drainage indicates the underlying cause of the fistula.

Emphasis is placed on the adjunct position of the technique. Cytology is not intended to replace any diagnostic method. It is most reliable in the detection of tumors arising from transitional cell epithelium. In my hands no such statement can be made about "hypernephroma."

⁴ Albrecht, P. *Arch. f. klin. Chir.* 77: 1073, 1905.

⁵ Shainoff, J. G., and Sala, A. M. *Am. Jour. Ca.*, 28: 1, 1936.

results in extravasation into the perivesical and retroperitoneal spaces or ischio-rectal fossa. Rupture below the urogenital diaphragm is likely to result in subcutaneous extravasation into scrotum, penis, lower abdomen or perineum. Rapid infection of extravasations in any of these areas is the rule and prompt operation is required.

Early definitive surgery In all cases, diversion of urine by cystostomy and drainage of extravasation are required. If possible, restitution of urethral continuity should be attempted at the time of first operation. Subsequent urinary extravasation and local sepsis result in scarring and deformity which greatly increase the difficulty of later repair. Strictures that develop after primary repair are usually benign, of large caliber, and easily controlled with sounds. Those resulting from treatment by diversion of the urine alone without use of a splinting catheter are consistently more severe. Of 30 cases reported by Robinson, Culp, Suby, Reiser and Mullenix managed primarily without use of a splinting catheter, the majority required further surgery.

The principles of primary treatment are 1) diversion of urine by suprapubic cystostomy, with prevesical and perivesical drainage, to save life, 2) provision of an indwelling catheter to serve as a splint, 3) some type of surgical approximation of the damaged tissues. A number of refinements of these maneuvers are possible.

In some cases, notably those of partial rupture of the posterior urethra, if a splinting catheter can be placed in the urethra no further operative repair is required. The catheter is left in place for at least 2 weeks. This treatment was used in 35 of the 100 cases of urethral wounds reported by Robinson and his associates. Excellent results, requiring no further surgery, were obtained in 25. In the other 10 extensive defects were present and fistulas developed which required later closure. Poole-Wilson reported 16 cases of rupture of the posterior urethra treated only by cystostomy and splinting catheter, of whom 11 required no other operative treatment.

If the prostate is displaced upward traction may be applied to a Foley catheter to hold the urethral fragments in approximation. This method has been reported on favorably by Conger, Lewis and Vermooten.

The displaced prostatic urethra may also be held in apposition to the torn membranous urethra by a suprapubic operation devised by Leadbetter. After cystostomy two heavy traction sutures on straight needles are placed on either side of the urethra through the substance of the prostate and led beneath the symphysis out through the perineal skin just behind the scrotum where they are tied over pads.

Occasionally it is possible to suture the prostatic apex to the triangular ligament suprapubically.

If an open perineal wound exists or if the wound involves the bulbous urethra primary perineal repair of the urethra should be attempted, after local debridement over an indwelling catheter. The surgical approach to the bulbous urethra is direct. Approaches to the prostatic and membranous urethra do not differ from those used in perineal prostatectomy. Delayed primary closure or second-

of anesthesia to be used for children in such operations, the amount of general anesthetic agent necessary can be reduced considerably and many times probably advantageously whenever it is possible either to apply a local anesthetic agent to the mucous membrane of the urethra or to infiltrate the skin and underlying tissues with a dilute solution of a local anesthetic agent, such as 0.5 per cent solution of procaine or metylocaine.

For a long time I have considered that the effect produced by preliminary medication followed by local anesthesia combined with light general anesthesia constitutes good balanced anesthesia. I still believe that this is true.

If, moreover, electrocoagulation is to be used during operation, the question of fire and explosion at once becomes very important, so that it is imperative to eliminate the use of inflammable and explosive agents as much as possible. In such an instance it would be important perhaps to use rectal anesthesia with pentothal sodium instead of ether. If that were done, it follows that one would have gone a step beyond what I have called "balanced anesthesia" and would have employed preliminary medication, rectal analgesia and nitrous oxide-oxygen anesthesia, with or without infiltration anesthesia. For those who prefer ether anesthesia, anesthesia may be induced and maintained with ether given by the drop method or with the gas machine. Each time the electrocoagulation device is to be employed, the anesthetist discontinues the administration of ether by the drop method and removes the mask. After the mask has been removed for a minute or two, there is little danger of damage to the patient from fire and explosion.

Those who do not use electrocoagulation may utilize any anesthetic agent, such as cyclopropane or ethylene. As the child becomes larger—it is about the age of 10 years or more—a point is reached at which, generally speaking, either intravenous anesthesia with gas and oxygen or intravenous anesthesia plus curare in small doses can be used. It is well to remember that curare requires about ten minutes to exert its maximal effect, and that this fact becomes important when large doses of curare are used. For example, for the ordinary patient the maximal effect of 1 or 2 cc of curare could hardly be said to be dangerous, but when a large dose is used the maximal effect continues to develop. Then the result can be dangerous. Fortunately, there is an antidote for curare, namely, Tensilon. The antidotal effect is exerted within 15 to 30 seconds when the antidote is given intravenously. Therefore, it is important that such an antidote be readily and quickly available.

It has seemed to me that girls at about the age of 17 years are more sensitive to pain under the influence of intravenous anesthesia than they may be at any other period of their life, particularly when incision in the skin is made. On the other hand, they are the very patients who most appreciate intravenous anesthesia and its lack of unpleasantness. On the other hand, patients at or near this age usually are robust enough to tolerate pain more than are many older people. My impression is, then, that despite the foregoing, the problem of anesthesia for patients of or near this age is not very great.

ANESTHESIA FOR PATIENTS 19 TO 70 YEARS OLD

The average adult person more than 19 years old but less than 70 years old constitutes a considerable problem in anesthesia. There are several reasons for

Poole-Wilson recommends tying the end of the urethral splinting catheter closed, while the cystostomy functions. The patient may then be evacuated with only one catheter attached to a bottle. The penis and perineum may be covered with a large sterile dressing and thus kept dry.

Itstitution of urethral continuity is impossible at the first operation, treatment must be limited to control of hemorrhage, preservation of tissue, and diversion of urine. Alignment of the fragments and secondary repair may be attempted when conditions permit.

In a case reported by O'Heeron, urethral obstruction resulted from a perineal hematoma. This was managed successfully by use of an indwelling catheter alone.

Complications and late surgery. If primary surgical repair of a urethral wound has been possible, sustained observation for stricture is required. Periodic dilatation with sounds may be necessary. Urethrography with opaque medium gives accurate information on the location and extent of postoperative scarring.

When primary repair can not be undertaken or is unsuccessful, urethrograms are a necessary part of study before secondary surgery is attempted. Such cases require excision of the stricture and of any existing urinary fistulas, with an attempt at reconstruction of the urethra after establishment of suprapubic cystostomy. Details of operative attack vary with each case. The urethral defect after excision of the stricture, may be great enough to require a graft. MacLean and Gerrie, in 2 cases, successfully reconstructed the posterior urethra by fixing a tubular graft of split thickness skin between the severed ends of the urethra about an indwelling catheter.

Recto-urethral fistula will sometimes heal spontaneously. Successful operative closure was accomplished in 2 cases of prostatic-rectal fistula by Poole-Wilson. The fistula was approached, excised and closed through the usual inverted V perineal incision. The rectal defect was invaginated and closed with two layers of sutures.

Lewis has successfully adapted the operation of Young and Stone for late repair of recto-urethral fistula due to war wounds and reported its use in 13 cases with favorable results. In this operation, the anal sphincter is dilated, the mucosa freed from it, and the rectum mobilized after division of the middle hemorrhoidal vessels until the rectal fistulous opening can be brought outside the anal margin without tension. The fistula is excised and the urethra repaired transversely, extramucosally. If a stricture has been present before operation an indwelling catheter is left in place. The advanced rectum after excision of the cuff containing the fistula, is fixed in place with stay sutures and the remaining mucosa approximated to the marginal skin. Drains are placed locally if necessary and a suprapubic cystostomy established.

The presence of bullets or shell fragments in the prostate or prostatic urethra may occasionally cause symptoms some time after injury. Pousson reported intermittent urethral obstruction of ball-valve type due to a bullet in the prostatic urethra 9 months after injury; the patient developed inability to void except when lying down. The bullet was located with sounds and by x-ray and removed suprapubically. Maurer and Prather have reported a case of urinary

to the name of the anesthetic agent or the procedure as to the person who uses it and how skillful he is in the use of it

ANESTHESIA FOR PATIENTS MORE THAN 70 YEARS OLD

The most outstanding difference between anesthesia for patients more than 70 years old and anesthesia for those 19 to 70 years old is that for the older group much smaller doses of the anesthetic agent are effective in a comparable operation. I have seen a patient 90 years old maintained in satisfactory anesthesia for 2 hours for a transabdominal operation, whereas a patient half that age would not have been maintained in satisfactory anesthesia for more than 30 minutes. Naturally, patients in this group are fewer than those in either of the foregoing two groups because of the limiting factor of extreme age, but on the other hand, it is well known that conditions referable to the urinary system are commoner among elderly people than among younger persons. Probably there are fewer congenital anomalies to be alarmed about among patients older than 70 years than there are in younger patients.

NEW ADVANCES AND TECHNIQUES

The present-day broad choice of anesthetic agents, the new advances in knowledge and special techniques and the remarkable progress that has been made in the last 25 years in the training of anesthesiologists have altered the picture very materially. Nowadays, urologists usually have ready access to a qualified anesthesiologist, so that they do not have quite the problem that existed a quarter of a century ago. At the Mayo Clinic the Section on Anesthesiology has had a very pleasant as well as valuable association with the urologists and with the surgeons who do urologic surgery. On the basis of rather considerable experience over the last 25 years, I should say that the results of present-day methods in the hands of trained anesthesiologists, working together with skilled urologists, have produced an example of teamwork that all of us can look upon with considerable satisfaction.

The late Dr. Ballenger was always developing new ideas in his field, and I am sure he would approve of my making some reference to the future of anesthesiology from the standpoint of its definite benefit to urologists and their patients. At the 1950 meeting of the American Medical Association in San Francisco, Dr. R. G. Bickford and associates¹ demonstrated a device for regulating the administration of anesthetic agents that was actuated by the electroencephalographic pattern made by the brain waves of the patient. This gave us a new concept of levels of anesthesia that were different from any that had been thought of before. I am sure the device and the technique have given and will in the future give us much needed information that should improve the production of anesthesia in general, and particularly among those patients for whom anesthesia ordinarily would be regarded as a bad risk.

¹ Courtin, R. F., Bickford, R. G. and Fieulencor, Albert Jr. The classification and significance of electroencephalographic patterns produced by nitrous oxide ether anesthesia during surgical operations. *Proc. Staff Meet. Mayo Clin.* 25: 197-206, 1950.

In civil practice, primary reconstruction of skin defects is often possible after avulsion of the skin of penis or scrotum. In suitable cases this may also prove possible in the field. Split thickness skin grafts have been successfully applied to the shaft of the penis. Testes may be transplanted beneath the skin of the thighs and subsequently returned to normal location beneath the pedicle grafts thus begun.

Because of the high regenerative power of scrotal skin, healing often occurs after its partial destruction without the need for secondary plastic procedures. In other cases satisfactory secondary closure of scrotal defects can be done using only undermining and relaxing incisions.

If primary repair of defects is not attempted, débridement and suitable local treatment are required to produce a clean granulating surface after which plastic procedures are selected to meet the requirements of the case.

Secondary reconstruction of the damaged anterior urethra and penis presents problems not differing materially from those encountered in the treatment of hypospadias.

Irumkin, working with Russian army casualties, reported that he was able to reconstruct the penis using an abdominal skin tube into which rib cartilage had been transplanted. Details of technique are not given in sufficient detail to permit appraisal of the method though good results are reported.

In patients in whom castration was required because of war wounds, subcutaneous implantation of pellets proved to be a convenient and satisfactory means of replacement of testosterone.

Simon reported a case of hematuria and urinary retention developing three years after gunshot wounds of the back. A rifle bullet was found impacted in the anterior urethra which could be expressed after meatotomy. Prather reported a meatal stricture occurring 3 months after debridement of a penile wound. This could not be controlled with sounds but was cured by excision of the stricture and revision of the meatus.

CONCLUSIONS

The majority of war wounds of the kidney are complicated by abdominal visceral injury and a considerable number by associated thoracic wounds. Laparotomy is indicated when combined renal and abdominal wounds are suspected. The kidney may be approached transperitoneally, through the flank, or through a combined thoraco-abdominal incision. In most kidney wounds, renal exploration, débridement, hemostasis and drainage are the only measures required. In some renal repair is possible. Nephrectomy is reserved in the early case for uncontrollable hemorrhage or massive destruction or infarction of kidney tissue.

In ureteral wounds, best results are obtained by diversion of urine by pyelotomy or nephrostomy and early re-establishment of ureteral continuity before carrying has resulted. Intubation technique end to end anastomosis, or uretero-vesical anastomosis can be used successfully according to the characteristics of the injury.

STREPTOMYCIN AND PAS TREATMENT OF GENITO-URINARY TUBERCULOSIS

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The Veterans Administration Research Group for Genito-Urinary Tuberculosis has treated 228 cases with chemotherapy alone. Treatment was judged successful only if the tubercle bacilli were eradicated from the urine. This may have been too rigorous a criterion, perhaps it should have been enough that the disease stopped progressing, even though the urine did not become completely negative.

RESULTS OF SHORT-TERM TREATMENT

Figure 1 shows a comparison of the effectiveness of four dosage regimens. The heaviest black line indicates the results with 2 gm streptomycin daily for a period of 4 months. Sixty-seven per cent had converted the urine to negative by the end of treatment, but after a 2 year follow-up, the percentage of success had fallen off to 45 per cent. There was loss of vestibular function in all patients of this 2 gm group. The next lower line represents the results with a less toxic regimen of 1 gm streptomycin daily for 4 months. The results were not as good initially (48 per cent success), but after 2 years the percentage of success was of the same magnitude as with 2 gm streptomycin. Next, a trial was made with the streptomycin reduced to 1 gm for 42 days, but with this regimen the results were completely unsatisfactory. It has been abandoned. Recently a group of patients have been tried on a combination of streptomycin 1 gm and PAS 12 gm every day for a 90 day period. The initial results again were of the same magnitude as with streptomycin alone (70 per cent success) but when the drugs were stopped, the percentage of successful conversions began to fall off sharply. These figures brought attention to the fact that short courses of treatment (up to 4 months) were not sufficient to permanently sterilize most tuberculous lesions.

SIZE OF RENAL LESION

When these figures were examined more closely, it was found that the success of treatment was related to the size of the renal lesion. Figure 2 shows the relationship of size of renal lesion to the ability to successfully convert the urine.

Read at annual meeting, American Urological Association, Chicago, Ill., May 24, 1951.
This study is one part of a co-ordinated large scale program of investigation into the effects of streptomycin on tuberculosis of all types, now being conducted by the Veterans Administration, The Army and The Navy. Since their Veteran patients will be followed indefinitely by the Veterans Hospitals, they present an unparalleled opportunity for long term follow up.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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impaired by the lack of circulation to such an area. This helps to explain the difficulty in sterilizing large, fibrous, tuberculous lesions.

FOUR YEAR RESULTS

Figure 4 shows a group of 25 patients who were treated with 2 gm streptomycin daily for 4 months, and who have been followed 4 years. The small kidney lesions continued to do well (7 successes out of 9). The very large kidney lesions did uniformly badly in point of converting to negative. The medium-sized lesions did fairly well (3 successes out of 8). Two of the patients with large lesions (fig. 4, patients 19 and 24) stayed negative for 2 years before breaking down and becoming positive again. Another patient (fig. 4, patient 14) remained negative

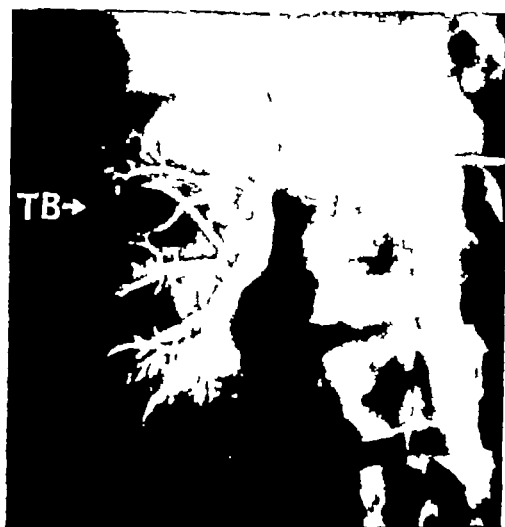


FIG. 3. Renal arteriogram of tuberculous kidney. Arterial vessels are deficient around fibrocaseous lesion in upper middle calyx. This helps to explain failure of blood borne drugs to effectively permeate fibrous lesions. Arteriogram by Dr. Willard E. Goodwin, Los Angeles.

for 4 years before his medium-sized kidney lesion finally became active again and began to discharge tubercle bacilli into the urine. This lesion was then removed by partial nephrectomy.

FOUR YEAR SURVIVAL

The remarkable thing about this group of patients, some of whom are living on one tiny fragment of one kidney, is that none of them have died of uremia. The only patient who is dead (fig. 4, patient 11) died of a heart attack at the age of 60, after being negative for 2½ years. This percentage (96 per cent) of 4 year survivals begins to make it appear that even a short (4 months) period of streptomycin treatment may have made the course of the disease more benign than formerly. Figure 5 shows a comparison of various dosage regimens upon medium-sized lesions only. The results with 2 gm streptomycin daily were fair (50 per cent) after 2 years, but the remaining tubercle bacilli were completely resistant to streptomycin. When alternate courses of PAS and strepto-

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bacilli throughout the treatment period. Since the resistance to streptomycin is deferred, bacteriostasis may persist long enough, with this plan, for healing to take place. This dosage plan prolongs the beneficial effect of treatment indefinitely. PAS 3 gm 4 times every day, and streptomycin 1 gm every third day, are now given for a period of at least 1 year. If pyuria is still present after 1 year, the treatment is carried on for a second or even a third year. Light work may be permitted after the first 6 months. This plan defers the development of streptomycin resistance, it controls symptoms, it is relatively nontoxic, it may check the progression of the disease and permit time for healing.

The idea of giving streptomycin only every third day seems irrational at first glance, but it has proven very effective in a large series of pulmonary tuberculosis cases. It is based on the fact that PAS, like the sulfa drugs, is bacteriostatic and must be given continuously for six or eight cell divisions of the tubercle bacilli before it becomes completely effective. Streptomycin, however, can get in its total effect in a single injection, and may be bacteriocidal. It is

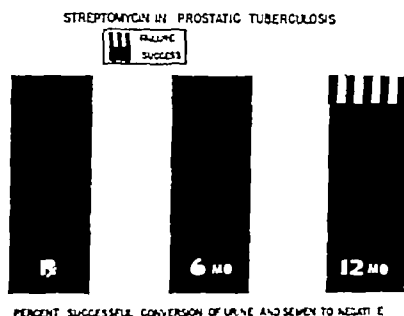


FIG. 6. Prostatic lesions which were causing urine or semen to be positive (rare) usually converted to negative urine. Prostatic nodules did not disappear, however. (See fig. 7.)

most effective just after each bacterial cell division. The greatest advantage of this new plan is the fact that the tubercle bacilli remain sensitive to streptomycin, despite the treatment.

PROSTATIC LESIONS

Figure 6 shows the results in cases where the urine was positive for tubercle bacilli because of prostatic foci which were discharging organisms. The results in converting the urine to negative were excellent (90 per cent). In some cases, however, a large tuberculous nodule in the prostate eventually broke down and began to discharge tubercle bacilli again. These nodules, as shown in figure 7, did not decrease in size after streptomycin treatment. In the rare case which does persist in causing the urine to be positive from such a solitary prostatic lesion, despite chemotherapy, total prostatectomy may be advised under cover of PAS and streptomycin.

EPIDIDYMAL TUBERCULOSIS

All tuberculous nodules in the epididymis were removed as soon after diagnosis as the patient's general condition would permit. The vas deferens was ex-

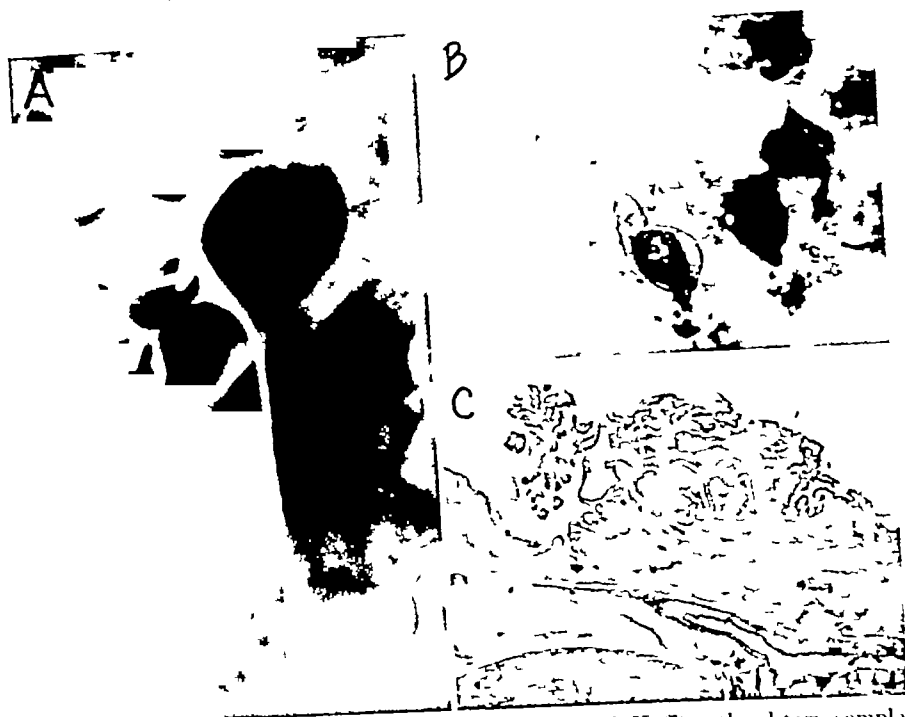


FIG. 2. D. C., a 44-year-old white man (case of Dr. Frank Huff) with solitary complaint of painless hematuria on one occasion. *A*, persistent filling defect in right pyelogram. *B*, type of cell found in right urinary sediment. *C*, low power view of entire tumor (1.5 cm. by 0.5 cm.).

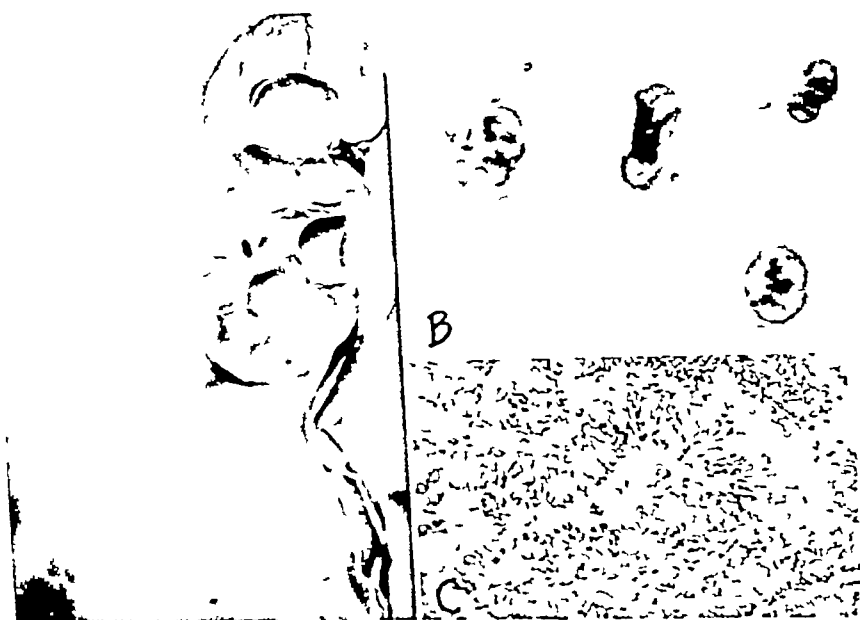


FIG. 3. A. D., a white man, 65, had a bladder tumor resected 5 years prior to admission. He had a filling defect in ureter. *A*, filling defect in uretrogram. *B*, cells in urine. *C*, 14 fr. counter below filling defect. *C*, microscopic field of tumor.

weeks. For instance, if the patient is very ill with tuberculosis when first seen, streptomycin may be given at the rate of 0.5 gm. every 6 hours for a period of 1 week and PAS may be given by clysis or infusion at the rate of 20 gm. every 12 hours. Once the patient's acute condition is under control the dosage may then be reduced to PAS 12 gm. daily by mouth, and streptomycin 1 gm. intramuscularly every third day. A similar intensive program may be given from 1 to 7 days at the time of dangerous operations such as partial nephrectomy for tuberculosis. This may reduce the intense hazard of military or meningeal dissemination from the operation. After the first postoperative week the dosage should be reduced to PAS 12 gm. daily and streptomycin 1 gm. every third day.

CONCLUSIONS

Very small renal lesions responded well to 4 month courses of chemotherapy alone. Medium sized and large lesions responded poorly. Four year survival was conspicuously good (96 per cent) among 25 cases of bilateral renal tuberculosis. Heminephrectomy is again being tried for tuberculosis under "cover" of chemotherapy.

Unilateral, active, destructive renal tuberculosis, visible in the pyelogram, where the innocent kidney shows no pus cells and no tubercle bacilli in the ureteral urine, is still best treated by nephrectomy. The operation is covered by at least 3 weeks of therapy with PAS 12 gm. and streptomycin 1 gm. daily. It is our feeling at this writing that solitary tuberculous kidneys, or bilateral active tuberculous kidneys, are best treated by one or more years of combined therapy. Our present regimen consists of PAS 3 gm. 4 times every day, and streptomycin 1 gm. in one injection every third day. This plan defers considerably the development of resistance.

Tuberculous epididymitis was treated surgically.

Tuberculous prostatitis usually converted to negative urine but rare refractory cases were treated by total prostatectomy.

Promising new drugs are being developed, but streptomycin and PAS are the optimum combination at this writing.

Our bacteriologist Milton Goldman, head nurse Lydia R. Sechler and her staff, our secretary Miss Alfreda Jastremski, illustrators Shapiro, Barlow and staff, and the Departments of Pathology, Roentgenology, Medicine, and Urology have been most helpful in this work.

We wish to express our appreciation to Consultant Dr. Archie L. Dean for sponsoring this presentation.

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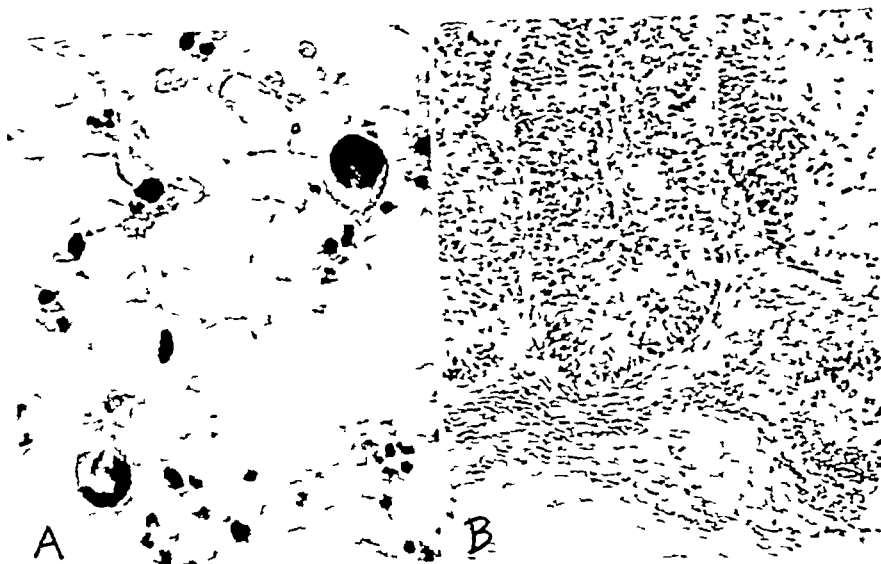


FIG. 6 Same case as figure 5. *A*, cells in left ureteral specimen. *B*, microscopic field of tumor.

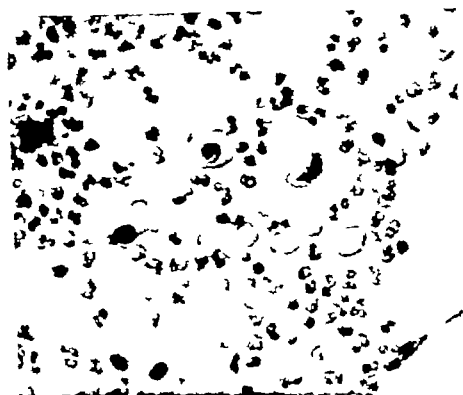


FIG. 7. *A. R.* a white woman aged 33 had a partial cystectomy for infiltrating transitional cell carcinoma. Six months postoperatively, suprapubic wound would intermittently drain small amounts of urine. It was difficult cystoscopically to determine whether infection or residual neoplasm was present. Cells in suprapubic drainage indicated residual neoplasm and patient later succumbed to disease.



FIG. 8. *A. D.* a white female. *A*, representative of tumors of bladder tumors. *B*, cells from bladder urine.

not as yet demonstrable, and before massive disseminations by way of the renal venous circulation have led to a generalized tuberculosis. Even without streptomycin, nephrectomy in very early renal tuberculosis offers better than an 80 per cent chance of a cure. With streptomycin added the results are further improved.

A complete and final cure should be reported only after the following criteria have been observed: 1) Tubercle bacilli are absent from the urine, 2) the leukocyte count on the urine is zero, 3) palpation of the genitalia is negative, 4) urinary symptoms are absent, 5) no extra-urinary tuberculosis is demonstrable.

Ten year follow-up. The disappearance of the organisms from the urine, while a favorable sign, is not an absolute criterion of cure. We have seen them reappear as late as 2 years after the termination of streptomycin therapy. The leukocyte count (number per H P F) on the urine is just as important and is usually roughly proportional to the extent of the lesion. If palpable genital lesions are still present, further trouble may often be expected.

Streptomycin is a valuable agent in the treatment of genito-urinary tuberculosis. It is not a substitute for surgery, which should be performed upon the already well established indications. In pyelographically negative renal tuberculosis, it usually cures the disease. In inoperable cases it prolongs life and alleviates symptoms, but rarely cures.

DR FRED H. VAN GULIK (Amsterdam, Holland). The treatment of urogenital tuberculosis is expensive in your country, but it is even more so in Holland, because of the fact that almost all of these drugs have to be imported from dollar areas. As a consequence, we have to be very careful in choosing the patients for such treatments.

Notwithstanding these financial problems, which became quite serious after we lost our Dutch East Indian colonies—nowadays commonly called Indonesia—we have been able to treat 60 patients in the University Hospital of Amsterdam suffering with urogenital tuberculosis. Of these 60 patients, 31 were followed during a period of 4 to 16 months, with an average of 9 months. About 10 patients were first treated with streptomycin during a period of 30 to 60 days, 1 gram daily, without results. We then put them on a regimen of PAS, 12 to 20 gm daily, also without results.

They were then treated with a combined dose of streptomycin, 1 gm daily, and 20 gm PAS daily, during a period of 120 days. All but one became negative.

Of a total of 31 patients thus treated, 3 remained positive, 2 became positive after having been negative for some time, up to the last follow-up, 26 patients out of 31 were negative.

I quite confess that our follow-up period is too short to draw definite conclusions.

In conclusion, I would say that we are very satisfied with the results obtained with these patients with the combined treatment of 1 gm streptomycin and 20 gm PAS daily during 120 days. Although we know of good results having been reported with a PAS treatment only, we are much inclined to believe that

CHOICE OF ANESTHETIC METHODS FOR UROLOGIC OPERATIONS IN VARIOUS AGE GROUPS

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One cannot hope to cover all phases of this broad question within a reasonable length of time, and so I shall endeavor to confine my remarks to illustrative points. So far as possible then, I shall present a generalized picture of my opinions based on my own experience only. Members of the three groups to which I referred in the title of this talk are children of no specific age, adult persons to the age of 70 years and persons of advanced years—70 or more.

ANESTHESIA FOR CHILD UROLOGIC PATIENTS

I suppose the most common use for rectal anesthesia in the field under consideration is to render the child unconscious of a painful procedure, such as cystoscopic examination. After trying a variety of methods, I have become convinced that anesthesia produced by pentothal sodium administered rectally is the most convenient and satisfactory method. If the dose of the drug thus employed is not completely effective by itself, it is a simple matter to supplement it by an inhalation anesthetic, such as nitrous oxide and oxygen, in which case the oxygen content of the breathing bag will be ample both to maintain the necessary stage and plane of anesthesia as well as to oxygenate the patient properly. Pentothal sodium has been colored slightly for rectal use to distinguish it from the intravenous preparation. Three grams of pentothal sodium is dissolved in 30 cc distilled water and 0.2 cc of the 10 per cent solution is administered for each pound of body weight. This is a minimal dose. It will be more effective in a patient who has had preliminary medication than one who has not had it. The preliminary medication which seems to be adequate and safe for children is between $\frac{1}{2}$ grain (0.032 gm) and $1\frac{1}{2}$ grains (0.1 gm) of nembutal administered by rectum 15 minutes before operation or examination. The child falls asleep rather rapidly—usually in less than ten minutes—and he will remain sleepy, but may respond to painful stimuli for two or three hours after the operation or examination has been completed. However, I must point out that if this procedure is carried out in the morning, by the middle of the afternoon the patient usually will exhibit little or no evidence of having had the drug.

If an operation is to be carried out, such as for removal of a Wilms tumor or for correction of cystopty of the bladder, then, generally speaking, preliminary medication is mentioned above plus the hypodermic injection of $\frac{3}{100}$ grain (0.00022 gm) of atropine sulfate and the subcutaneous injection of $\frac{1}{16}$ grain (0.004 gm) of morphine sulfate followed by inhalation anesthesia with nitrous oxide, oxygen and ether have been very safe and satisfactory in my own experience. Without wishing to enter the controversy as to what forms of anesthesia should not be used, perhaps I may exclude spinal anesthesia and intravenous anesthesia. Let me point out, however, that irrespective of the particular method

only. It appeared to be localized. Removal of the superior pole was performed in 1945. There were no untoward results. The patient had streptomycin for only 2 weeks during this period, since it was somewhat difficult to obtain, and one used it sparingly. He had a serous discharge from a small fistulous tract for a period of only 2 month's time, and this healed spontaneously.

He was examined periodically, and urine cultures were obtained every two to three months during the intervening years' time. Unfortunately they always revealed tubercle bacilli, by guinea pig inoculation or by culture, so that nephrectomy was done 1 year later even though calyceal details were excellent. Giant cells and small tubercles were sparsely distributed in the renal parenchyma.

Unfortunately, I hadn't the temerity to continue following him nor did I anticipate the institution of prolonged streptomycin therapy. Nephrectomy was performed 1 year later. Healing of the microscopic areas of involvement might have occurred on continued therapy. Tuberculous meningitis became evident 3 years after nephrectomy. He was treated more than 1 year with combined streptomycin-PAS therapy but succumbed eventually to the disease.

DR. GEORGE E. SLOTKIN (Buffalo, N. Y.): We have here a condition which I believe is more serious than cancer, and I wish to congratulate Dr. Lattimer upon his most excellent presentation, and his concurrence in the viewpoint that we have a very serious disease.

Because of this seriousness, no matter what we hit this bacillus with, we do it for the benefit of the patient, whether it is a course of streptomycin and PAS for a year or 2 or 3 or 5 years, makes no difference, as long as we can get this patient eventually free of bacilli.

We still believe that the kidney which has lost its blood supply cannot be treated successfully with any method of therapy. On the other hand, we believe that, because this is a bilateral disease to begin with, these patients are entitled to chemotherapeutic treatment. It has been shown by Dr. Lattimer, and concurred in by Dr. Lloyd, that the blood supply to the lesion is an important factor. With a lack of blood supply, chemotherapeutic agents cannot properly reach the lesion.

Results have been stated by Dr. Lloyd—in which I concur—that it is the scar which eventually develops which is important in the cure or the isolation of tuberculosis, and for that reason I believe that the treatment which I suggested some 3 years ago still is a very valuable adjunct, and still a very valuable part of our armamentarium. Diasone, one of the sulfonimides, facilitates the formation of the scar which is necessary in the healing of tuberculosis.

My treatment today is almost similar to that which we instituted 2 or 3 years ago. Our series, of course, is much smaller than that of Dr. Lattimer's. He is certainly to be congratulated again on his larger series and excellent results. Our series is only composed of a little over a hundred patients.

Our treatment consists of half a gram of streptomycin a day to prevent an vestibular reaction, plus 2 cc of moogrol or, if the patient resents the injections after 2 or 3 courses of treatment, then the admission of diasone, one of the

this. For one thing, patients of this age group are the most numerous. They may have many problems, not all urologic, and some of which are very serious. Social and economic factors complicate the physician's responsibility in respect to the survival of these particular patients, because many of them have families who depend on their earnings. In this group—both men and women—for ordinary cystoscopy the application of a local surface anesthetic agent has been the time-honored method. However, since the introduction of intravenous anesthesia many urologists prefer that their patient be anesthetized with an intravenous anesthetic agent. Such a procedure certainly seems to please the patient, especially the female patient. In fact, regardless of the patient's sex, when multiple examinations or operations are required, the average person probably would prefer intravenous anesthesia.

For these patients between the ages of 19 and 70 years it is desirable to consider keeping the dose restricted to a minimum. This is accomplished by preliminary medication and by the supplementary inhalation of 50 per cent nitrous oxide and 50 per cent oxygen while the intravenous anesthetic agent is being administered. Electrocoagulation can be used safely when this combination is used. Should relaxation by any chance be required, as for example in operations on the kidney, on the ureter or on the bladder, a small amount of curare will produce it. It is seldom necessary to use an endotracheal tube for these particular patients. The fact that the patient is in the so-called kidney position does not interfere with the airway, as a rule. In operations on the bladder and ureter the patient often is in the Trendelenburg position, which actually tends to minimize the respiratory difficulty which might come about because of obstruction of respiration by the tongue.

The patient undergoing operation for removal of a pheochromocytoma may exhibit some startling changes in blood pressure, values indicative of shock may be reached suddenly after the anesthetic agent has been administered for approximately 15 minutes. The condition of such patients obviously is so different from that of the ordinary patient that if the physician will bear in mind the specific lesion concerned it will obviate some embarrassment or even difficulty. Sometimes the administration of an anesthetic agent has even been of differential diagnostic value in cases in which the real lesion was an adrenal tumor producing effects which had caused the erroneous diagnosis of essential hypertension to be made.

Spinal anesthesia has been a very satisfactory procedure for a large percentage of patients in this age group who undergo transurethral procedures. Sacral block anesthesia can be used. There is a difference between the results obtained from spinal anesthesia and those obtained from sacral block anesthesia in that when the spinal procedure is used perforation of the bladder is not recognized as soon as it is when sacral block anesthesia is used. Priapism, which interferes with the use of the cystoscope, has been encountered during sacral block anesthesia, but so far as I know it has not occurred during spinal anesthesia.

The problem of anesthesia for patients 19 to 70 years old is not very hazardous as a rule. Although care should be exercised whenever any anesthetic agent is to be used. It is seldom desirable, however, to use rectal anesthesia for these patients. It is perhaps unnecessary to say that importance attaches not so much

USE OF TERRAMYCIN IN NONSPECIFIC URETHRITIS

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One of the obstinate problems confronting urologists is that of chronic non specific urethritis. Before the advent of sulfonamides and antibiotics most cases were treated with dilatations, irrigations and instillations. Prior to 1941, the gonococcus, even if not found, was still blamed as the causative organism. During World War II many thousands of "early morning drops" were examined for gonorrhea without success. During and since the war, nonspecific urethritis has become a well-recognized entity and energetic attempts to "cure" these patients have been made.

In a study of 2000 American soldiers serving in the Pacific theater, 2.97 per cent contracted gonorrhea, whereas, 12.4 per cent had nonspecific urethritis. Wilcox reports that in his cases of nonspecific urethritis studied, 52.3 per cent gave a previous history of venereal disease.

The average patient suffering from urethritis has become disgruntled and impatient. This is especially true if he has not been promiscuous in his sexual behavior. After using the armamentarium of drugs at our disposal, we often try to discourage the patient in returning to our office or clinic because we have nothing further to offer him.

We are apt to forget some of the good old procedures which were used prior to the advent of the "miracle" drugs. In many offices today, the routine 3 glass test, smears and cultures have been discarded and have been supplanted by the hope of prompt response to antibiotic therapy. However, only a relatively low percentage will respond to such therapy, and what is to be done with the large group of nonresponders remains a problem.

The procedures to be used on the patient are often determined by his work, time available for therapy, and ability to carry out "home" treatments. The beneficiaries of Marine Hospitals are usually unable to follow a long drawn out course of therapy. Thus it has behooved us to devise a simplified routine which would enable the patient to continue on duty. To prescribe medication while not under our observation was considered inadvisable since we had no control of toxicity or complications.

The senior author made a study of the bacterial flora in cases of non-specific urethritis. There was a large group of organisms but *Staphylococcus albus*, *Staphylococcus aureus*, diphtheroids and *Serratia* were predominant.

After ruling out gonorrhea by smears and cultures, the patients were often given a course of penicillin and streptomycin and on occasions aureomycin. Depending on the response, many required additional treatment with chloromycetin and terramycin. It has also been customary to treat the obstinate cases with instillations and dilatations.

Recently in evaluation of our treatments in non-specific urethritis showed that the patients returned entirely too frequently and for a long period of time.

This device, which employs both electro-encephalographic² and electrocardiographic tracings, has been developed so that it is definitely helpful in management of the patient who constitutes a bad risk because of cardiac disease.

Cerebral anoxia, which occasionally can develop for one reason or another, can be dealt with for the most part by the intravenous use of serum albumin as suggested by Seldon and co-workers,³ for the purpose of reducing the edema of the brain that is associated with such a condition. Three or four doses of serum albumin, each dose consisting of about 100 cc, and each dose given at an interval of 4 to 5 hours, should be employed.

Recently, Missa and associates⁴ have developed a so-called plastic needle, to which the tube attaches on the outside of the introducing needle. This fills a need that had not been satisfied before. It is a very useful device. Faulconer and Ridley⁵ have developed a device for obtaining very elaborate information as to what is going on within the gas machine during anesthesia and what is going on within the patient. This device permits very accurate examination of the patient's reactions to drugs and techniques, and it should be important in advancing the science of anesthesiology materially.

Diagnostic and therapeutic block techniques^{6, 7} for the discovery of pain pathways and for the control of pain have been developed. Roentgenograms are used to assist in placing the point of the needle in the correct site for injection of the local anesthetic agent and ammonium sulfate, alcohol and 6 per cent solution of phenol in water. Much progress has been made and much more no doubt will be made in the control of pain, a prospect welcomed alike by those in the practice of general medicine as well as urologists who may be faced with the problem of the control of pain.

In both the prophylactic and the therapeutic treatment of shock^{8, 9} there are available now in limited quantity certain agents which in the future should be more widely available. I mention such agents as dextran, periston and gelatin, which act as plasma volume expanders. I think that urologists will find them to be very useful, as I have in my own experience.

² Mayo, C. W., Bickford, R. G. and Faulconer, Albert Jr. Electroencephalographically controlled anesthesia in abdominal surgery. *J. A. M. A.* **144**: 1081-1083, 1950.

³ Seldon, F. H., Faulconer, Albert Jr., Courtin, R. I. and Pino, D. M. Postanesthetic encephalopathy. The postulation of cerebral edema as a basis for rational treatment. *Proc. Staff Meet., Mayo Clin.* **24**: 370-374, 1949.

⁴ Missa, D. J., Lundy, J. S., Faulconer, Albert Jr. and Ridley, R. W. A plastic needle. *Proc. Staff Meet., Mayo Clin.* **25**: 413-415, 1950.

⁵ Faulconer, Albert Jr. and Ridley, R. W. Continuous quantitative analysis of mixtures of oxygen, nitrous oxide and ether with and without nitrogen. *Anesthesiology* **11**: 269-275, 1949.

⁶ Lundy, J. S., Adams, R. C., Seldon, F. H., Pender, J. W., Faulconer, Albert Jr., Paulson, J. A., Ridley, R. W., O'Brien, J. I. and Courtin, R. I. Annual report for 1949 of the Section on Anesthesiology. Including data and remarks concerning blood transfusion and the use of blood substitutes. *Proc. Staff Meet., Mayo Clin.* **25**: 503-509, 1950.

⁷ Lundy, J. S., Adams, R. C., Seldon, F. H., Pender, J. W., Faulconer, Albert Jr., Paulson, J. A. and Ridley, R. W. Annual report for 1948 of the Section on Anesthesiology. Including data and remarks concerning blood transfusion and the use of blood substitutes. *Proc. Staff Meet., Mayo Clin.* **24**: 384-400, 1949.

⁸ Lundy, J. S., Gray, H. K. and Crank, W. McK. Dextran in supportive therapy with elements on periton and gelatin. *Arch. Surg.* **61**: 53, 60, 1940.

⁹ Lundy, J. S. New solutions. *Minnesota Med.* **34**: 21-23, 1951.

improvement. The other forms of treatment still have their place. Advice to the patient as to forcing fluids, abstinence, and preventing of stripping the urethra to look for a discharge is very important.

SUMMARY

Nonspecific urethritis is a definite entity.

Using 2½ per cent solution of terramycin hydrochloride as urethral instillations in conjunction with simultaneous dilatation and massaging of the urethra, a high per cent of the resistant cases responded with one to five treatments.

Terramycin instillations should be used in resistant cases because of its ability to attack a wide bacterial spectrum.

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to negative. These are 2-year follow-up results. When small kidney lesions were treated, the results were very good (75 per cent success) even after 2 years. (Small kidney lesions were those too small to be visible in the pyelogram.) When medium-sized kidney lesions were treated (medium-sized kidney lesions were those where only one calyx showed a definite erosion), medium results were

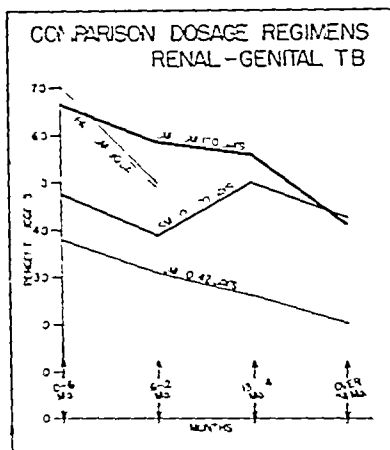


FIG. 1. Percentage of success in eradicating tubercle bacilli from urine. After 2 years, there was no significant difference between results from 2 gm, 120 days, and 1 gm, 120 days. The 1 gm, 60 days regimen was less toxic, however.

EFFECT SIZE OF RENAL LESION ON SUCCESSFUL CONVERSION OF URINE TO NEGATIVE



FIG. 2. In cases with small lesions, too tiny to show in pyelogram, patients did well after 2 years of follow-up. Medium-sized lesions, involving only one calyx, stayed negative in one-half the cases. Huge lesions showed no 2-year conversions.

obtained (50 per cent). Very large kidney lesions gave very poor results, with no permanent conversions of the urine to negative.

Figure 3 is an arteriogram of a kidney with a medium-sized tuberculous lesion. It was taken by Dr. Willard L. Goodwin of Los Angeles. It is apparent that the arterioles are deficient around the area of tuberculous fibrosis and especially in the upper middle calyx. Since streptomycin and PAS are best carried to the lesion by the blood vessels, it is apparent that healing would be greatly

strictures developed on the basis of the infection McVay and associates¹⁰ isolated *Brucella* from 3 of 34 prostates of persons who had at the time no symptoms of brucellosis but had previously had symptoms compatible with the disease.

Hardy and co-workers¹¹ reported a case in which the patient's initial symptoms were those of cystitis, later, orchiepididymitis developed and a diagnosis of brucellosis was made on the basis of a very high agglutination titer.

Reports of pyelonephritis with good evidence favoring *Brucella* as the etiologic agent are rare. Cazeneuve¹² described a case in which hematuria occurred during the acute phase of the disease. Other European writers¹³ have mentioned pyelitis as a complication early in the disease. Hardy and co-workers¹¹ in 1936 were the first to report cases in which the initial symptoms were suggestive of renal tuberculosis but in which the disease proved to be brucellosis on isolation of *Brucella* from the urine. This possibility was brought to attention again by Clark¹⁴ in 1939 who reported a case of recurrent pyelitis and cystitis which responded to therapy for brucellosis and was considered of *Brucella* etiology. Since textbooks on urology make no mention of the possibility of pyelonephritis due to *Brucella*, and a monograph on infections of the kidney mentions the subject only briefly, it is felt that the possibility of the condition is not generally recognized. It is thought, therefore, that the following cases of brucellosis of the urinary tract should be of interest.

REPORT OF CASES

Case 1—A farmer aged 47 years came to the Mayo Clinic in June 1947, because of urinary frequency, nocturia and suprapubic distress of 1 year's duration. He had had acute brucellosis 5 years previously with symptoms which lasted 4 months. Since that time the patient had experienced short episodes of fever (100F) approximately three times yearly.

The results of physical examination were essentially negative. Examination of a voided specimen of urine disclosed pyuria, grade 4. Cultures of the urine on eosin-methylene blue agar, hormone blood agar and brain broth were sterile. Examination of the urinary sediment stained both by the Gram method and for *Mycobacterium tuberculosis* yielded negative results. A culture of the blood for *Brucella* was sterile for 15 days and then was overgrown by *Micrococcus*. Agglutination of the serum for brucellosis occurred in a dilution of 1:200. The urea content of the blood was 38 mg. per 100 cc. Routine blood counts were normal and the serologic reaction for syphilis was negative.

A plain roentgenogram of the urinary tract disclosed fine calcific shadows scattered throughout the renal parenchyma. By means of excretory urography, dilatation and clubbing of all the calyces were demonstrated (fig. 1 a and b).

¹⁰ McVay, I. A., Guthrie, F., Michelson, I. D. and Sprunt, D. H. *Proc. Soc. Exper. Biol. & Med.* 69: 607-608, 1948.

¹¹ Hardy, A. V., Jordan, D. F., Borts, I. H. and Hardy, Grace C. *Nat. Inst. Health Bull.* (No. 158) 1931, p. 75.

¹² Cazeneuve, H. J. *Bull. Soc. path. exot.* 4: 91-98, 1911.

¹³ Stenzel, K. G. *Ztschr. f. Urol.* 25: 267-271, 1931.

¹⁴ Hardy, A. V., Jordan, C. F. and Borts, I. H. *J. A. M. A.* 107: 559-564 (Aug. 22) 1936.

¹⁵ Clark, A. I. *J. Urol.* 42: 249-256, 1939.

mycin were given, the results were unsatisfactory. It was apparent from these data that there was very little hope of permanently eradicating the tubercle bacilli from the urine from any kidney lesion large enough to be definitely visible

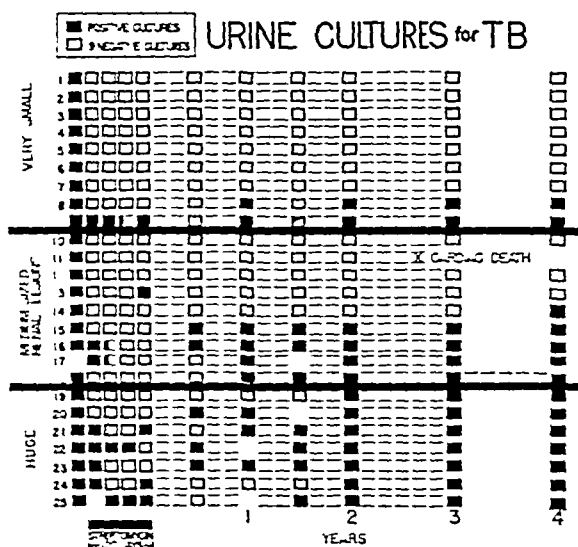


FIG. 4. Four year follow up on 25 men with renal tuberculosis. Most small lesions remained negative. Majority of medium sized lesions relapsed to positive. Patient 14 relapsed after being negative for 4 years. All large lesions have relapsed, patients 19 and 24 after being negative for 2 years. None has died of uremia, even though several have huge bilateral renal lesions.

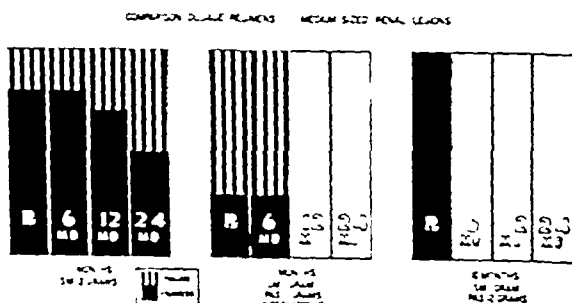


FIG. 5. One hundred twenty day regimens (left) converted 57 per cent to negative, but when streptomycin was stopped, more and more of the organisms burst forth again, it is time again to wait on. Intermittent therapy (center) was unsatisfactory. Current regimen (right) is 1 year of streptomycin (every third day) and PAS 12 gm daily. This plan defers the development of resistance.

in the pyelogram. Short, intensive courses of treatment appeared to wall off tuberculous lesions only temporarily. After treatment was stopped, the organisms burst forth again, this time in resistant form. A new dosage plan has therefore been evolved.

NEW DOSAGE PLAN

Two periods of treatment (1 to 3 years), with a 3 day interval between doses of streptomycin are now being tried. The urine usually stays free of tubercle

recurrent attacks of urinary frequency, dysuria, and nocturia. At that time the results of physical examination and laboratory studies were essentially the same as at the previous visit. In addition, the calcium and phosphorus content of the blood was 9.8 and 2.8 mg, respectively, per 100 cc. The urinary tract as visualized by excretory urography was similar to that described previously.

Vesical urine was injected into guinea pigs. One month after injection the guinea pigs were tested with tuberculin and negative results were noted. Two months after injection, necropsy was performed and no evidence of tuberculosis was noted. However, lesions of the spleen were discovered which by means of culture* on hormone blood agar were found to be due to *Brucella* and not to *Mycobacterium tuberculosis*.

A diagnosis of chronic pyelonephritis due to *Brucella* was made and the patient was advised to return for definitive treatment, which he did in May 1948. Urologic investigation at that time showed little change except for possible increased calcification in the kidneys. Retrograde pyelograms disclosed severe bilateral chronic pyelonephritis. Vesical urine and urine from each kidney, collected by ureteral catheterization, were cultured for *Brucella*, and *Brucella melitensis* was recovered from each specimen. The results of routine cultures of the urine and study of the urinary sediment stained by Gram's method remained negative.

Therapy consisted of 6 gm. of sulfadiazine administered orally in addition to 1.2 gm. of streptomycin administered intramuscularly, both in divided doses, during each 24-hour period. Such therapy was continued for 2 weeks. During therapy the streptomycin in the blood reached a concentration of 27.5 micrograms per cubic centimeter and the sulfadiazine level remained around 12 mg per 100 cc. Examination of a specimen of urine revealed a concentration of streptomycin of 245 micrograms per cubic centimeter.

Six days after institution of treatment the results of cultures of the urine for *Brucella* became negative. The urinary symptoms gradually abated. Six weeks after discontinuance of therapy the results of cultures of the urine for *Brucella* were still negative. Cystoscopy at that time showed mild chronic cystitis, and microscopic examination of a catheterized specimen revealed pyuria, grade 2.

* Hormone blood agar as used at the Mayo Clinic is prepared by adding whole human blood to hormone agar to make a 10 per cent mixture. The hormone agar is prepared as follows:

1. Dissolve 15 gm. of agar in 1 liter of distilled water and allow to cool to 50 to 60°C.
2. Add 500 gm. of beef heart (ground and all fat removed). Bring to a boil and cook slowly for 20 minutes.
3. Filter through an ordinary round flour sieve.
4. Allow agar and meat on the sieve to become evenly spread out so that the mixture acts as a filter, and again pour the filtrate through it.
5. Add 10 gm. of peptone (Bacto), 5 gm. of sodium chloride and 1 gm. of gelatin (Bacto).
6. Boil for 10 minutes. Correct to pH 7.6.
7. Add 2.5 gm. of dextrose. Tube in 12 cc. amounts and sterilize 20 minutes at 15 pounds pressure.

The inoculated plates are incubated at 37°C in an atmosphere of 8 to 10 per cent carbon dioxide. The small, oval, gray, moist colonies of *Brucella* usually make their appearance in four or five days, if growth has not occurred after three weeks, the results are considered to be negative and the plates are discarded. Final identification and typing are based on the lack of fermentation, production of hydrogen sulfide, presence of urease, agglutination with known specific antiserum and the reaction to the dye inhibition test using thionin and basic fuchsin.

terized and the operation "covered" by streptomycin and PAS for at least 3 weeks.

OTHER DRUGS

No practical substitute for streptomycin has yet been found. Dihydrostreptomycin is comparable to streptomycin in effectiveness but there has been some deafness reported following its use. We therefore prefer ordinary streptomycin. Mycomycin is as yet too unstable. Viomycin and neomycin are too toxic. Neomycin has been used for instillation into bladders of patients whose organisms are resistant to streptomycin. In patients who cannot tolerate streptomycin, tibione in a 100 mg. capsule, can be given once daily in combination with PAS. Nausea and liver damage are the chief hazards in the use of tibione.

DIFFICULTIES WITH PAS

PAS occasionally causes nausea or diarrhea sufficient to necessitate the use of less irritating proprietary preparations of sodium PAS such as 'enseals',



FIG. 7. Prostatic nodules did not change after chemotherapy, and in occasional refractory cases total prostatovesiculectomy was indicated.

or effervescent tablets of 'propasa', which can be taken in ginger ale. PAS can even be given by cystis or infusion in doses up to 40 gm. per day. Infusion carries the risk of severe hemolytic anemia, however. If a patient is completely unable to tolerate PAS, then a sulfone called promizole (2 gm. 4 times daily) can be substituted.

STREPTOMYCIN RESISTANCE

Every effort is made to keep resistance from developing. Streptomycin is given only every third day in an effort to deter the development of resistance, and streptomycin is never given alone. It is always given in combination with either PAS or promizole. This helps to delay the development of resistance.

However, streptomycin does appear to exert some beneficial effect even after the patient's organisms are reported completely refractory to streptomycin by the laboratory. It is possible that some of the organisms present are still sensitive to the drug even in these resistant cases. Once resistance has developed, however, the organisms never become sensitive again as far as has been determined.

INTENSIVE CHEMOTHERAPY

Under certain special circumstances it may be advisable to initiate treatment with an increased dosage of streptomycin and PAS for a period of 1 or 2

smaller. A catheterized specimen of urine contained pus cells but no bacteria could be found either by means of routine cultures or by microscopic examination of the sediment stained by Gram's method.

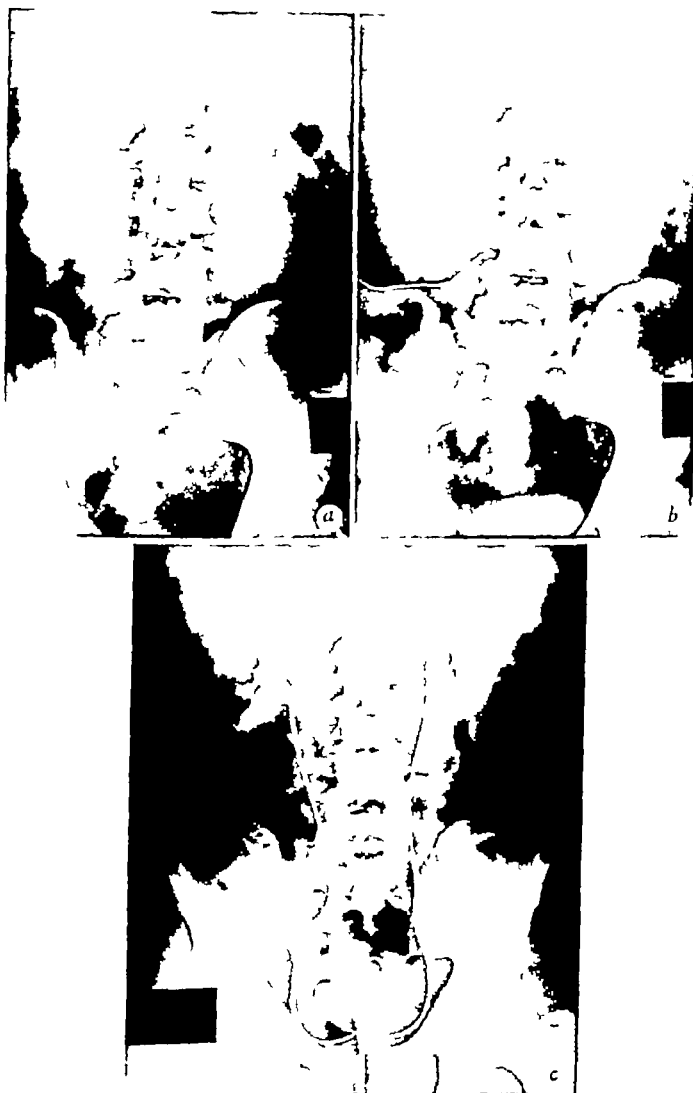


FIG. 2 Case 2 *a*, Plain roentgenogram of urinary tract *b*, Excretory urogram *c*, Bilateral retrograde pyelogram

Brucellosis of the urinary tract was suspected. The urine was cultured on hormone blood agar plates under 10 per cent carbon-dioxide tension and incubated at 37°C. After 4 days tiny colonies appeared which were shown to be *Brucella suis*. Urine was injected into guinea pigs and when they were examined at necropsy 8 weeks later, nodular lesions were found in the spleen, these lesions were proved by culture to be due to *Brucella suis*. The agglutination reaction for brucellosis was positive in a dilution of 1:1,000.

DISCUSSION

DR FREDERICK A. LLOYD (Chicago, Ill.) Drs. Lattimer and Deim are to be commended for continuing their excellent work. The great advantage of the combined therapy with PAS is that the development of streptomycin resistance is largely prevented. Since the generation of the tubercle bacillus is approximately $1\frac{1}{4}$ to $3\frac{1}{2}$ days, and since streptomycin is merely a bacteriostatic agent, the multiplication of the organisms can be prevented by giving 1-2 gm. streptomycin twice a week with a full daily dose of PAS. This combined intermittent therapy shows great promise and makes it possible to carry on the treatment for a year or longer. The natural defensive forces of the body then have a better chance to cure the disease.

We have treated 27 cases of genito-urinary tuberculosis with combined therapy using a daily dose of 1 gm. streptomycin for 90-120 days. The results appeared to be slightly better than with streptomycin alone, and genital lesions responded somewhat better.

Streptomycin has now been used in the treatment of genito-urinary tuberculosis for a period of over 5 years. It seems fitting, therefore, to evaluate at this time the exact place of this antibiotic in our therapeutic armamentarium. It has become apparent to all conscientious and well qualified therapists in all fields of tuberculosis that streptomycin is not the final answer to the disease. When used wisely it is of great aid, when used unwisely, it is dangerous. The stumbling block to the cure of the disease is the necrotic lesion. The therapeutic ideal is to convert this into a fibrous scar which does not contain tubercle bacilli. This is the only irreversible lesion. So far this has not often been possible, and here too streptomycin has failed utterly. In genito-urinary tuberculosis the healing of mucous membrane lesions with streptomycin therapy alone has led to a temporary remission of symptoms and a false sense of security. False recoveries have been common.

We have removed 24 tuberculous kidneys and given a full course of streptomycin starting 2 weeks before surgery. In 21 of these or in 87 per cent the follow-up was negative for an average period of 33 months. Considering that 7 had early tuberculous lesions in the opposite kidney and that in 7 genital lesions of sufficient severity to require unilateral or bilateral epididymectomy were present, this is indeed an amazing result.

If one were to compare the different forms of therapy in unilateral caseous cavernous renal tuberculosis the results would be as follows:

- 1) Conservative. Sixty per cent are dead in 5 years. Most survivors are in miserable condition after this time.
- 2) Streptomycin alone. Fewer than 25 per cent are cured.
- 3) Nephrectomy alone. Fifty to 60 per cent are cured.
- 4) Nephrectomy plus streptomycin. At least 70-80 per cent cures.

Renal tuberculosis is a deadly disease. The time to cure it is when the renal mass is small, when the opposite kidney is still intact, when genital lesions are

tract, of course, acid-fast bacilli may be found in the urinary sediment by proper staining methods. If the results of such staining are negative it will be necessary to resort to cultures in order to distinguish tuberculosis from brucellosis.

Brucellosis of the urinary tract may closely resemble chronic nonspecific pyelonephritis. In both diseases the symptoms may be identical. Cystoscopy and pyelographic studies may yield similar findings in both conditions. Calcification of some calyces with dilatation of others and the deposition of calcium occur in chronic pyelonephritis just as in brucellosis. In the former disease, however, organisms which belong to the colon-typhoid group may usually be demonstrated in the urine by suitable staining methods or by cultures. In some instances of chronic nonspecific pyelonephritis, however, no bacteria can be detected in the urine by routine methods. In order to distinguish between the two diseases it is necessary to culture the urine specifically for *Brucella*.

Brucellosis of the urinary tract should be suspected in all patients complaining of urinary symptoms whose past history reveals previous systemic infection due to *Brucella*. Acute cystitis and roentgenographic evidences of pyelonephritis with deposits of calcium are suggestive signs. The presence of pyuria in the absence of bacteria when routine staining and cultural methods are employed lends further suggestive evidence. Positive blood agglutination reactions for *Brucella* at high titers, for example, 1:400, provide corroborative evidence. It must be remembered that brucellergen skin testing and a "therapeutic trial" of *Brucella* vaccine therapy may greatly increase the agglutinins, the agglutination reaction has uncertain diagnostic value if performed after either of these procedures. A definitive diagnosis is established by isolation of the *Brucella* organisms on suitable media.

Therapy with a combination of dihydrostreptomycin and sulfadiazine in our cases produced prompt and gratifying relief of the patient's symptoms. Mild pyuria and cystoscopic evidence of cystitis persisted in both cases. As might be expected the roentgenographic evidences of pyelonephritis remained unchanged. The rapid eradication of the *Brucella* organisms following institution of therapy and their failure to reappear following cessation of therapy were surprising. Such responses are not ordinarily observed in the treatment of deep seated chronic infections of the urinary tract of nonspecific nature.

A newer and more successful method of treating brucellosis has recently been advanced.¹⁶ This consists of the daily administration of 750 mg. of aurcomycin every 6 hours together with 1 gm. of dihydrostreptomycin every 12 hours. Such therapy is continued for 12 to 14 days in cases of acute brucellosis and for 21 to 28 days in cases of chronic or complicated disease. This combination of drugs appears to be superior to the combination which we employed.

¹⁶ Herrick, W. E. and Barber, T. L. Proc. Staff Meet., Mayo Clin. **24**: 138-145, 1949.

PAS should be combined with streptomycin. In some cases which have recently come into our hospital, we have given 1 gm streptomycin every third day instead of every day, to try to diminish the resistance to streptomycin.

DR D C MALCOLM (Los Angeles, Calif.) Dr Lattimer and Dr Lloyd have met the challenge of tuberculosis, that ubiquitous marauder of the genito-urinary tract. They are extending and furthering the methods of treatment espoused by Albarrin and Wilbolz and developed by Gilbert Thomas, Nesbit, T. Leon Howard and many others.

Chemotherapeutic and antibiotic modalities have improved the lot of these most unfortunate patients. These medications should be resorted to prior to surgical extirpation of tissues so involved by tuberculosis that restoration of function is most unlikely.

The possibilities for future development are not inconsiderable. Dr Lloyd contends that nephrectomy of one involved kidney should be performed relatively early, but the urologists of Seaview Hospital abandoned this concept, which they had formerly supported. My personal view is that hematogenous dissemination is no more likely from a kidney than from other tissues. Tubercle bacilli are frequently lurking in other areas.

Lack of response to sanatorium regimen, and chemotherapy, with increase in symptoms as well as development of calyceal erosion, are the salient indications which warrant removal of the kidney. Certainly, many of those with definite bilateral renal involvement do quite well on continued PAS therapy.

Six of 10 patients treated with streptomycin or streptomycin and PAS have failed to reveal *Mycobacterium tuberculosis* by culture or guinea pig inoculation during the past 4 year period of time. Two of these six had slight erosion of one calyx. Two had a single remaining kidney following removal of the opposite one a few years previously for tuberculosis. Two have continued having mild chronic pyelonephritis which is non-specific.

Sixty per cent of the patients had no symptoms, but presented cellular elements in the urine which proved to be due to tuberculous renal involvement.

Semb of Oslo, Norway has proposed that we regard renal tuberculosis as a disease process which is similar to pulmonary tuberculosis. Resection of portions of an involved kidney has been proposed and performed.

Albarrin had stated that renal tuberculosis does not heal spontaneously, but Medlar controverts this inclusive statement.

Semb reported 14 patients operated on by resection of the superior, inferior, or even the mid calyces with localized ulcerative tuberculous lesions; five of these were free of tubercle bacilli for a period of 9 months after operation. This concept has been employed to a minimal degree in America.

It was my privilege to call for a 26 year old patient in 1945 who had previously had an orchectomy for tuberculous involvement. There were no genito-urinary tract symptoms, but tubercle bacilli were detected on a urinary sediment near from the left kidney with none from the right.

Semb. A retrograde pyelogram revealed a 4 mm erosion of the superior calyx.

biotic was used as control. All tubes were incubated at 37°C and the resulting growth was noted grossly at regular intervals.

RESULTS

The bacteriostatic effects of terramycin and polymyxin B alone and in combination on 16 representative strains of gram-negative bacilli responsible for infection of the urinary tract were determined. The results are summarized in table 1, which shows the fraction of the amount of each antibiotic sufficient to prevent growth of the organism when used in combination of that necessary for

TABLE 1. *Synergistic effects of polymyxin B and terramycin on urinary tract pathogens*

MICRO-ORGANISMS		FRACTION OF MINIMAL GROWTH INHIBITORY AMOUNTS OF BOTH ANTIBIOTICS USED IN COMBINATION OF THAT OF EACH USED SINGLY			
		Terramycin		Polymyxin B	
		24 hours	120 hours	24 hours	120 hours
<i>E. coli</i>	(3853)	$\frac{1}{2}$	$\frac{1}{16}$	$\frac{1}{16}$	$\frac{1}{4}$
	(3791)	$\frac{1}{2}$	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{16}$
	(3776)	$\frac{1}{2}$	$\frac{1}{8}$	$\frac{1}{2}$	$\frac{1}{4}$
	(3634)	$\frac{1}{2}$	$\frac{1}{16}$	$\frac{1}{2}$	$\frac{1}{8}$
	(3646)	$\frac{1}{2}$	$\frac{1}{3}$	$\frac{1}{4}$	$\frac{1}{8}$
<i>A. aerogenes</i>	(3961)	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{1}{4}$
	(3824)	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{4}$
	(3818)	$\frac{1}{4}$	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{4}$
	(3625)	—	$\frac{1}{4}$	—	$\frac{1}{4}$
<i>Paracolobactrum</i>	(3692)	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{2}$
	(3911)	$\frac{1}{2}$	—	$\frac{1}{4}$	—
<i>P. aeruginosa</i>	(3598)	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$
	(3611)	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{4}$
	(3613)	—	$\frac{1}{2}$	—	$\frac{1}{16}$
	(3934)	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{4}$
<i>P. morgani</i>	(3697)	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$	$\frac{1}{2}$

each antibiotic alone. It is evident that terramycin and polymyxin act synergistically against *E. coli*, *A. aerogenes* and, to a lesser degree, against *Pseudomonas aeruginosa* and *Proteus morgani*.

The synergistic action was present, as may be noted from table 1, not only at 24 hours of incubation but also after 5 days. It should be stressed, however, that the absolute amount of terramycin causing growth inhibition was markedly greater on the fifth day of observation than on the first day. This is due to the fact that terramycin under the conditions of these experiments undergoes change resulting in loss of activity. For example, where 1.5 to 6 µg of terramycin were effective with the majority of these strains in producing growth inhibition for 24 hours, from 25 to more than 50 µg were required after 5 days of incubation. Two series of experiments revealed that the increase in the minimal concentration

sulphurous which is used in the treatment of leprosy, 2 gm a day, half a gram four times a day. The only difficulty with diasonone is that you must watch your patient so that secondary anemia does not develop. That is supplemented with 10 to 15 gm PAS, as Dr Lattimer has suggested.

Now, what is the purpose of PAS? The PAS has no real action on the bacilli, we have shown that, Dr Lattimer has shown that, everybody has shown it. But it prevents the resistance of the bacillus against streptomycin, and therefore should be added to the regimen.

May I repeat that anything that is used in the treatment of this case, anything that is going to knock out this armor-clad bacillus which is very resistant, is a valuable part of our therapy. May I therefore suggest again a half gram of streptomycin a day, over several courses of treatment, 2 cc *moogrol* a day, 2 gm of diasonone if the patient cannot tolerate *moogrol*, in order to facilitate the scarification and softening up of the bacillus, making it more receptive to PAS and streptomycin with 10 to 15 gm PAS a day.

PAS is today available in an effervescent tablet made by Sharp & Dohme. It is a half-gram tablet, which can be given the same as any other effervescent tablet, and is more palatable and more readily given to the patient than the formula which heretofore existed.

PROGRAM, ANNUAL MEETING, WESTERN SECTION AMERICAN UROLOGICAL ASSOCIATION, HOTEL HUNTINGTON, PASADENA, CALIFORNIA, MAY 18-22, 1952

MAY 20

THE REASON BUCK'S AND COLLES' FASCIÆ ARE CLOSED SACS Miley B Wesson, San Francisco, Calif

DISCUSSION Edward Beach, Sacramento, Calif, Bernard Strauss, Los Angeles, Calif
ANTAGONISM BETWEEN BACTERICIDAL AND BACTERIOSTATIC ANTIBIOTICS IN TREATING UROLOGICAL CASES F H Redewill, San Francisco, Calif, and (by invitation) M M McIlwain, New York City and F H Redewill, Jr, Whittier, Calif

TESTS IN VIVO AND VITRO TO PROVE ANTAGONISM OF THE VARIOUS ANTIBIOTICS
DISCUSSION Paul Wedgewood, San Diego, Calif

SURGICAL AND HORMONAL THERAPY OF BENIGN AND MALIGNANT ANDROGENIC HYPERFUNCTION OF THE ADRENAL CORTEX Clarence V Hodges, Portland, Ore

DISCUSSION Franklin Farman, Whittier, Calif, H Spencer Hoyt, Monterey, Calif
ANASTOMOSIS OF VAS DEFERENS TO CORRECT POST-VASECTOMY STERILITY John W Dorsey, Long Beach, Calif

DISCUSSION Donald Charnock, Los Angeles, Calif Ernest Bors, Long Beach, Calif
AORTOGRAPHY AND RETROPERITONEAL OXYGEN IN UROLOGIC DIAGNOSIS Willard I Goodwin, Los Angeles, Calif (by invitation) and Robert C Walter, Los Angeles, Calif
EXTRAPERITONEAL PNEUMOGRAPHY Donald R Smith, San Francisco, Calif

DISCUSSION Thomas E Gibson, San Francisco, Calif, Donald Malcolm, Long Beach, Calif

ROUND TABLE DISCUSSION A J Scholl, Los Angeles, Calif, moderator, assisted by Herman Riddell, Los Angeles, Calif

MAY 21

PRESIDENT'S ADDRESS CONTINUED EDUCATION Paul A Ferrier, Pasadena, Calif

ROBERT V DAY LECTURE WHAT MAKES THE PROSTATE GROW? William Wallace Scott, Professor of Urology, Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, Md

DISCUSSION (Past Presidents) Dudley Fagerstrom, San Jose, Calif Archibald Hunter, Vancouver, B C, A M Meads, Oakland, Calif, and William Ross, Jr, Yakima, Wash

SPECIAL LECTURE TREATMENT OF CARCINOMA OF PROSTATE BY INTERSTITIAL IRRADIATION WITH RADIOACTIVE ISOTOPES Rubin H Flocks, Professor of Urology, in collaboration with H D Kerr, H B Flkins, D Culp, University Hospitals, Iowa City, Iowa

DISCUSSION Henry Jaffe, Director, Department of Radiation Therapy, Cedars of Lebanon Hospital, Los Angeles, Calif, and Carl F Rusche

TRANSVESICAL PROSTATECTOMY WITH PRIMARY CLOSURE McCleery Glazier, Los Angeles, Calif

THE SURGICAL TREATMENT OF PROSTATISM C D Goodhope, Seattle, Wash

DISCUSSION Arthur Cecil, Los Angeles, Calif, Miles Griffin, Berkeley, Calif, Samuel Bacon, Hollywood, Calif, Wilson Stegeman, Santa Rosa, Calif

POSTOPERATIVE URINARY INCONTINENCE James S Elliott, Berkeley, Calif

DISCUSSION Henry Weyrauch, San Francisco, Calif, B L Stewart, Los Angeles, Calif, Robert Plumb, San Diego, Calif

RESULTS OF NONSURGICAL TREATMENT OF EARLY CARCINOMA OF THE PROSTATE Robert W Barnes, Los Angeles, Calif

DISCUSSION Robert Prentiss, San Diego, Calif, Jack Nelson, Seattle, Wash
CARCINOMA OF THE PROSTATE, SELECTED CASES TREATED WITH FEMALE SEX HORMONES PRELIMINARY TO RADICAL PERINEAL PROSTATECTOMY Carl Hartwig, and J J Sullivan, Oakland, Calif

because of persistent urethral discharge. An endeavor was made to correct this situation. Oral and parenteral therapy often allowed the causative organisms to become resistant to the sulfonamide or antibiotic. Believing that nonspecific urethritis is primarily a local infection, why should we not attack it locally with higher concentrations of the drug of choice?

The diagnosis in our cases was confirmed in most instances by urethroscopy. There have been 102 resistant cases at our disposal since October 1950. One or more antibiotic was used in 30 cases without success, followed by dilatations of the urethra and instillations of 10 per cent mild silver protein. After 3 months of weekly instillations, there were 12 of the 30 patients remaining under treatment. We then instituted the use of terramycin in 5 per cent solution, 10 cc being instilled in the urethra followed by dilatation while the drug was still in contact with the urethral mucosa. Massage of the urethra over the sound permitted the urethral glands to come in contact with the terramycin. After withdrawing the sound the penis was clamped for 10 minutes, after which the patient was instructed to withhold urination as long as he could. Dilatations of the urethra are valuable in stretching the small ducts of the glands along the urethra thereby allowing these glands to drain adequately. The glands are usually the loci of infection in non-specific urethritis.

We believe that the absorption of terramycin used intra-urethally is not sufficient to cause a resistance of the micro-organisms to the drug. This factor may be important to certain patients at some future date.

After receiving several complaints from patients because the solution of terramycin caused considerable burning sensations the concentrations were made up fresh for each treatment and in 2 $\frac{1}{2}$ per cent. We instilled fresh solutions of 250 mg crystalline terramycin hydrochloride in 10 cc normal saline. This diminished any possibility of breakdown of the drug. The complaints of discomfort disappeared. The resistant cases showed remarkable response. Ten of the 12 patients have been discharged from out-patient care as cured. The other 2 patients have not responded completely but have shown a diminution in the amount of urethral discharge.

The remaining 72 cases in our study group have been given exclusive treatment of instillations of 2 $\frac{1}{2}$ per cent terramycin and dilatation of the urethra with massage. Sixty-six or 91 per cent have been discharged after receiving from one to five treatments averaging one to two per week. The remaining 6 cases are still under treatment and will probably require a re-evaluation of their status as to diagnosis and therapy.

Terramycin is one of the newer antibiotics which possesses potent antimicrobial activity. It is a very stable compound and maintains its potency for a prolonged period. It can be stored at room temperatures in the form of crystalline terramycin hydrochloride. It is highly effective against a wide range of pathogens including gram positive and gram negative bacteria.

The use of this new antibiotic as an adjunct in the local treatment of non-specific urethritis is supported by clinical results. Its use is not the entire answer to the problem but many resistant cases will show definite clinical recovery or

BRUCELLOSIS OF THE URINARY TRACT

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Brucellosis was described and clinically differentiated from malaria in 1814 by Burnett.¹ In 1887 the causative agent was isolated by Bruce after whom the disease is named. The literature concerning the systemic disease has grown voluminous and the Brucella group now includes the abortus, suis, and melitensis species. Reports of localized infections have been made only sporadically, but a monograph on brucellosis² discloses that practically every organ and tissue of the body has been reported to be involved in localized infection with Brucella.

The urinary tract would seem particularly vulnerable since at certain stages of the disease 50 per cent of patients with brucellosis may pass organisms in the urine, according to a British commission quoted by Keefer.³ In this country, Wainwright⁴ in 1929 found organisms in the urine of 20 per cent of patients infected with Brucella melitensis and 4 per cent of patients infected with Brucella abortus. Brucella organisms are not easily isolated from the urine, which explains the infrequent attempts at such isolation.

In the genito-urinary tract the testicles appear to be the organs most frequently infected with Brucella either with or without systemic manifestations of the disease. Some workers have reported that orchitis develops in 2 to 20 per cent of patients with systemic brucellosis.⁵⁻⁶ One wonders, however, whether orchitis is peculiar to certain regions of the country since Spink⁷ in Minnesota reported that he had not encountered this complication.

An interesting case of Brucella prostatitis was reported by Boyd⁸ who emphasized that to make certain of the diagnosis of chronic brucellosis it is generally necessary to find Brucella by culture, since there is no other infallible method. The literature is replete with case reports in which the diagnosis is open to question. Harris⁹ reported a case of proved Brucella prostatitis in which he felt that

¹ Read at annual meeting, North Central Section, American Urological Association, Milwaukee, Wis., October 13, 1930.

² Part II, In Cecil, P. F., A Textbook of Medicine, Ed. 7, Philadelphia, W. B. Saunders Co., 1947, p. 235.

³ Harris, H. J., Brucellosis (Undulant Fever), Clinical and Subclinical, New York, Paul H. Broer Inc., 1941, 280 pp.

⁴ Keefer, C. S., Bull. Johns Hopkins Ho., p. 35, 6-11, 1921.

⁵ Wainwright, C. W., Bull. Johns Hopkins Ho., p. 45, 143-171, 1929.

⁶ Part II, F. J. Calif. & W. Med., 38, 175-177, 1935.

⁷ Spink, A. G., J. Urol., 40, 201-207, 1938.

⁸ Boyd, W. W., Mich. J. Med., Dec., 24, 15, 1947.

⁹ Harris, H. J., J. Urol., 39, 717-721, 1938.

¹⁰ Harris, H. J., J. A. M. A., 110, 678, 1938.

retroperitoneal ganglia. Rarely, three so far, they have been reported in the thorax. There has been an association of cutaneous neurofibromatosis with the tumor in 5 per cent of the cases and many of these were multiple tumors. Most of the tumors have been benign, malignancy reported as 9 per cent by McKeith.¹ Few of these malignant cases had some hypertensive symptoms but most did not.

The symptom described as paroxysmal hypertension appears to be present in about one third of the cases of proven tumors. Paroxysmal hypertension by itself is not indicative of tumor of the chromaffin system. In fact it is more often due to many other conditions. It has been reported as occurring in eclampsia, lead poisoning, essential hypertension, nephritis, aortitis and vascular diseases and diseases of the nervous system such as epilepsy, hypothalamic lesions described as autonomic epilepsy, trauma and vascular damage to the brain or the meninges. Psychoneurosis or hysteria accompanied by some hypertension has presented many difficulties in determining whether or not a pheochromocytoma was present. These form the largest group that has been seen to attempt a differential diagnosis, and tumor has been most rare among them. On the other hand, when tumor has been identified and removed, the cases have been most erroneously previously treated as essential hypertension, cardiac neurosis, hyperthyroidism, diabetes mellitus or renal tumor.

When tumor has been present the following important differences have been noted. Most of the tumor cases had emotional stability. The paroxysms were most often precipitated by physical or mechanical causes, although anxiety may be a producing cause. Often there has been a recognizable preceding aura. Their pattern is most always the same, although they vary from patient to patient. The attack always was associated with anxiety, headache and followed by precordial and epigastric distress. Most of the patients, but not all may have a pounding of the heart, coldness and blanching of the extremities, some shortness of breath, some nausea or vomiting and in all profuse sweating occurs with cessation of the attack. Associated with the attack there is an elevation of the systolic and diastolic blood pressure, hypermetabolism and often an elevation of blood sugar and the appearance of glycosuria. The attacks are such as would be precipitated by a symptom-producing intravenous dose of epinephrine and norepinephrine. The variations seen most likely are and can be simulated by the relative amounts of these drugs when administered.

Persistent hypertension with or without paroxysmal crisis is more frequently the presenting symptom according to Green² who in a review of 51 cases states that only 14 had paroxysmal hypertension and 37 had a more or less continuous hypertension. It is the opinion of many workers in this field that no cases of hypertension should be subjected to any radical procedure such as lumbar dorsal sympathectomy without first excluding if possible the presence of pheochromocytoma by pharmaceutical methods. Widely quoted is Smithwick's³ finding that pheochromocytoma was found in 0.5 per cent of 1000 cases of hypertension.

¹ McKeith, R. Brit. Heart J. 6:1, 1944.

² Green, D. N. J. A. M. A., 131:1260, 1946.

³ Smithwick, R. H. Cited by Goldenberg, et al., J. A. M. A. 135:971, 1947.

Subacute diffuse cystitis, particularly evident about the trigone, and edema of the ureteral orifices were noted by cystoscopic examination. Retrograde pyelograms revealed narrowing of the infundibulum to the upper calyx of each kidney.

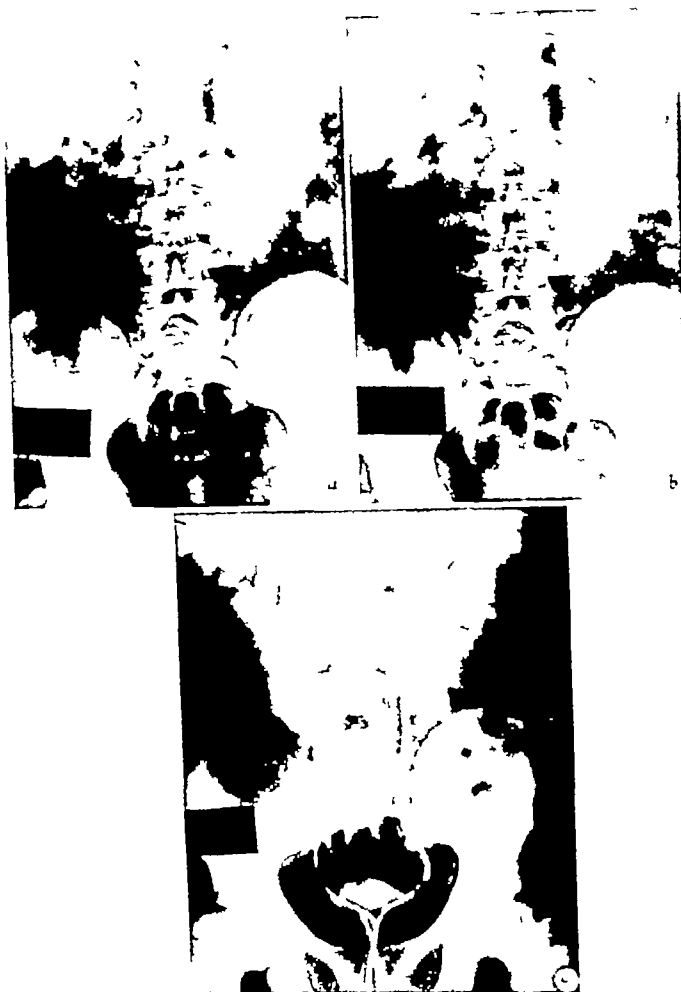


FIG. 1. *a*, Plain roentgenogram of urinary tract; *b*, Excretory urogram; *c*, Bilateral retrograde pyelogram.

and visualization of these calyces was impossible; calcitrization and dilatation of all the remaining calyces were noted (fig. 1 *c*).

A diagnosis of chronic bilateral pyelonephritis of indeterminate origin was made, and sulfadiazine was administered over a period of 10 days. Although suspected a diagnosis of brucellosis was not established. At the time of completion of therapy the patient's urinary symptoms had abated and he was dismissed from the clinic.

The patient returned for further investigation in January 1948, because of

psychoneurotics with hypertensive crises, elevations of blood pressure have been obtained by us with injections of histamine base. The rise was slower and the rise of more sustained type than seen with tumor. In a number of these cases no tumor was found on exploration.

Guarneri and Evans⁷ used mecholyl bromide in 25 mg. dose subcutaneously to incite a paroxysm of hypertension in a patient from whom a pheochromocytoma was removed. The use of this test showed that side reactions of mecholyl may occur with the injection. Aranow, Jr.⁸ suggested a modification of this test to include the preadministration of at least 0.01 gm. of atropine sulfate parenterally prior to the use of the mecholyl because untoward and perhaps fatal reactions may occur in patients in whom the parasympathetic effectors have not previously been blocked.

The intravenous injection of tetraethyl ammonium bromide has been reported by LaDue⁹ and his co-workers as producing a paroxysmal rise in blood pressure in a case with pheochromocytoma. The advantage of the test is that the extent of the rise may be controlled by changing the position of the patient. It is a longer acting agent than histamine and has been stated by Roth⁹ to be less reliable.

Of the three provocatives used it is believed by many of the reporters that histamine has been shown to be the more reliable and more often used.

The use of provocatives depends upon the precipitation of the hypertensive crises. Its safety would largely be determined by the status of each case. In young patients without as yet any marked vascular changes, and subject to frequent attacks, it has been of no more risk than the frequent attacks the patient has been experiencing. In cases with severe arterial changes as shown by retinal damage and in older persons, the test unless well controlled has some greater risk. Histamine has less side effects than mecholyl and apparently is more reliable than tetraethyl ammonium bromide and for these two reasons has been the preferred provocative to date.

ANTAGONISTS

Of the antagonist, benzodioxane (pyeredylmethyl-benzodioxane) introduced by Goldenberg¹⁰ and co-workers has been particularly useful in the presence of sustained hypertension. This drug introduced intravenously, 0.25 mg. per kilo body weight, has a predominantly depressor action in cases of hypertension and pheochromocytoma, and in hypertensives of other causes, had a predominantly pressor effect. Goldenberg and Aranow¹¹ have reported that it correctly indicated the presence of a tumor in 59 cases reported from various clinics. It has been reported as having failed to produce a significant fall in blood pressure in a few cases. There have been explanations offered as to these few failures but there has been a positive response associated with tumor in over 90 per cent of the cases reported. In a number of cases suspected of tumor but with a negative response

⁷ Guarneri, V. and Evans, J. A. *Am. J. Med.*, 4: 806, 1948.

⁸ LaDue, J. S., Murison, P. J. and Pack, G. T. *Ann. Int. Med.*, 29: 911, 1948.

⁹ Discussion, Calkins et al.⁵

¹⁰ Goldenberg, M., Snyder, C. H. and Aranow, H. Jr. *J. A. M. A.*, 135: 971, 1947.

¹¹ Goldenberg, M. and Aranow, H. Jr. *J. A. M. A.*, 143: 1139, 1950.

The patient returned 6 months after therapy generally improved although continuing to experience urinary frequency and suprapubic distress. Cultures of the urine for *Brucella* gave negative results and the agglutination titer in the test for *Brucella* had dropped from 1:200 to less than 1:50. The symptoms were ascribed to residual chronic cystitis, and local therapy was advised. Treatment consisted of 2 gm. of sulfadiazine given daily, which resulted in relief of urinary symptoms.

Case 2—A butcher aged 35 years, from southern Minnesota, came for examination in July 1947, because of recurrent infection of the urinary tract of 2 years' duration. During this period he had experienced attacks of urinary frequency, dysuria, hematuria, and pain in the right flank. He had noted easy fatigue, generalized aches and pains and malaise for one year prior to admission. A diagnosis of cystitis and prostatitis had been made and temporary relief of symptoms was gained by means of penicillin, sulfonamides, and prostatic massage. Twelve years prior to admission he had experienced an attack of brucellosis.

The pertinent findings on physical examination were questionable enlargement of the right kidney, enlargement of the spleen, and mild, generalized lymphadenopathy. Microscopic examination of a catheterized specimen of urine disclosed pyuria, grade 3. Studies of the urinary sediment stained by Gram's method and for acid-fast organisms were negative for bacteria. The results of routine cultures of the urine and cultures for *Mycobacterium tuberculosis* were negative. Urine was injected into guinea pigs and the animals were subsequently examined, but no evidence of tuberculosis was found. Examination of the expressed prostatic secretions revealed 20 pus cells per high-power field. The urea content of the blood was 48 mg. per 100 cc. Routine blood counts were normal. The agglutination reaction for brucellosis was positive in a dilution of 1:400.

The urinary tract was studied by cystoscopy, excretory urography, and retrograde pyelography. The pelvis and calyces appeared normal but extensive areas of calcification were noted in each kidney, particularly the right (fig. 2 a, b and c). Mild generalized cystitis was noted. Examination of the urine from the right kidney disclosed mild pyuria, pus cells were not found in the urine from the left kidney. The results of routine cultures of the urine were negative. A diagnosis of chronic, nonspecific pyelonephritis, prostatitis and cystitis was made. A course of prostatic massage was advised and given by the patient's home physician.

The patient returned in November 1947, because of a recurrence of urinary frequency, nocturia, and dysuria. Examination of the urine disclosed pyuria, and study of the expressed prostatic secretions revealed prostatitis. Stains of the urinary sediment were negative for bacteria and routine cultures of the urine were sterile. Prostatic massage and instillations of silver nitrate and mild silver protein (argyrol) into the prostatic urethra resulted in symptomatic relief.

The patient again returned, in July 1948, because of suprapubic distress, severe urinary frequency, dysuria, hematuria and pain in the right flank, he had also noted the passage of calcareous material in the urine. An excretory urogram revealed the appearance of the urinary tract to be unchanged as compared with the appearance one year previously, the vesical outline, however, appeared

the tumor or tumors completely relieves the patient of the symptoms and signs of the suprarenal sympathetic syndrome

A factor in the successful operation upon these tumors is the planning of the procedure. To date several adrenolytic agents have been used, first for diagnosis, and second, particularly for therapeutic effect in the operative handling of these cases. One is dibenamine, first used by Spear and Griswold¹⁶ and Hoch,¹⁷ and the second regitine reported by Grimson.¹⁸

Dibenamine (dibenzylbetachlorethylamine hydrochloride) is used in 5-7 mg per kilo of body weight given in an infusion of 300 to 500 cc of saline. It is administered slowly for 1 hour. The action is prolonged and it has frequent side effects. Its action is a sympathicolytic effect producing a prolonged depressor effect. Dibenamine has been used for diagnostic purposes because it will reduce the blood pressure dramatically with an effect that lasts from 24 to 72 hours. The reduction of blood pressure is not specific of pheochromocytoma because it will also reduce the blood pressure in other hypertensives inasmuch this drug is not only adrenolytic but is sympathicolytic. Because of its effect, it has been used for its beneficial effect upon the patient preoperatively. The result of the injections has been a lowering of the blood pressure with freedom from the other manifestations of hypertensive crises and the ability to rest and to receive and retain nourishment. In cases with severe symptoms the drug has been used several times with resting intervals between. During this period there was marked improvement in the cases so treated. Side effects may occur and temporary hemi-amnesia and hemiplegia have been reported, as has also tetany.¹⁸ The risk of these side effects would seem to limit the use of this drug to those severe cases in which the tumor has existed for a long time and are often emaciated and in which it is necessary to revive the individual before submission to operation. The operative procedures with dibenamine have been performed in the later part of the period of the depressor effect. While this effect is still present, manipulation of the tumor has been possible in a manner that probably would have been fatal without the sympathicolytic agent. Operation during the period of maximum depressor effect eliminates a diagnostic aid, namely the rise in pressure that occurs in the handling of tumor of pheochrome tissue. Also during this period the marked fall in pressure that may occur after removal of the tumor may not be reversed by any sustaining drug such as epinephrine or nor-epinephrine because of the effect of the sympathicolytic agent. There is a necessary regulation of the timing in the injection of this agent in relation to the operation. Enough effect must be present to allow the manipulation of the tumor but not too much to prevent the use of sustaining drugs. The successful use of this drug has been reported by Hoch,¹⁷ Cahill and Monteith¹⁸ and others. Unpublished reports upon its side effects have been commented upon.

Another adrenolytic drug has been reported by Grimson, C-7337 or regitine. This he used and reported upon its success as a diagnostic help and as a therapy.

¹⁶ Spear, H. C. and Griswold, D. *New Eng J Med*, **239** 736, 1949.

¹⁷ Hoch, G. J. *Urol*, **61** 473, 1949.

¹⁸ Cahill, G. F. and Monteith, J. C. *New Eng J Med*, **244** 657, 1951.

¹⁹ Grimson, K. S. Discussion Calkins et al.⁴

Cystoscopy disclosed scattered areas of acute inflammation involving particularly the entire right wall of the bladder. The left ureteral orifice could not be identified and in its site was an inflammatory cystlike structure, a specimen removed for biopsy was composed of inflammatory tissue. The vesical capacity was 100 cc. *Brucella* was cultured from a specimen of urine from the right kidney.

Therapy consisted of the administration of 4 gm. of sulfadiazine and 2.4 gm. of dihydrostreptomycin a day in divided doses, this treatment continued for 26 days. The level of sulfadiazine in the blood was maintained at about 12 mg. per 100 cc. and the level of dihydrostreptomycin varied from 27 to 64 micrograms per cubic centimeter.

Nineteen days after the institution of therapy, the results of cultures of the urine for *Brucella* were negative. The urinary symptoms rapidly abated and the vesical capacity increased to 175 cc. Cystoscopic examination, however, disclosed no change in the appearance of the bladder. Repeated cultures of the urine during a period of two months following cessation of treatment were sterile for *Brucella*. The urinary symptoms disappeared entirely and the vesical capacity increased to 300 cc. Mild pyuria persisted, however, and cystoscopy disclosed scattered areas of cystitis. Further therapy was not advised.

DISCUSSION

The delay in establishing a correct diagnosis in the first case was due to our unawareness of the fact that *Brucella* can produce pyelonephritis and cystitis. The diagnosis was established only after examination of the bodies of the guinea pigs into which the patient's urine had been injected in a search for tubercle bacilli. The lesions found in the spleen grossly resembled those of tuberculosis but no acid-fast bacilli could be found while cultures of the tissue revealed *Brucella*. Armed with this knowledge and noting the similarity of the clinical pictures, we were able to establish the correct diagnosis in the second case by specifically requesting that the urine be cultured for *Brucella*.

It is necessary to distinguish brucellosis of the urinary tract from tuberculosis and nonspecific pyelonephritis. The similarity between brucellosis and tuberculosis of the urinary tract is striking. Patients with either disease note severe vesical symptoms such as dysuria, strangury, hematuria and nocturia. Urinalysis in both diseases discloses pyuria, microhematuria, usually an absence of bacteria when the urinary sediment is stained by Gram's method and usually sterile cultures when routine culture media are employed. Cystoscopic examination in both conditions discloses acute inflammation, ulceration, and decreased vesical capacity. Pnelographic visualization of the upper part of the urinary tract in both diseases may depict clubbing of some calyces and dilatation of others, and small depositions of calcium. In brucellosis the deposits of calcium are numerous and are situated in relation to all the calyces, whereas in tuberculosis the deposits are less numerous and are usually situated in relation to one or two calyces. In brucellosis also affects the prostate and testicles, as has been reported in the literature, a differential diagnosis becomes more difficult inasmuch as tuberculosis frequently attacks these organs. In cases of tuberculosis of the urinary

removal of the tumor the blood pressure often falls to surprisingly low levels and this may be prevented by increasing the rate of flow of the nor epinephrine intravenous drip. Preoperative preparation with high salt intake and desoxycortosterone was effective in one case of pheochromocytoma in a Cushing's syndrome operated upon by us. The vascularity of some of the larger tumors makes movement difficult at times and requires immediate blood replacement. The operative risk is steadily falling with the improvements in preparation and immediate pharmacological therapy.

SUMMARY

The diagnosis of pheochromocytoma is made by

- a History and findings
- b Demonstration of excess pressor substance by an antagonist in persistent hypertension
- c Demonstration, if necessary, of the production of excessor or pressor substance by a provocative in a paroxysmal hypertension
- d Demonstration if possible of a tumor by x-ray

The treatment is operative removal. This is made more successful by

- a An androlytic or sympathicolytic agent to prevent the hypertensive crisis on removal of the tumor
- b A replacement sustaining hypertensive substance to correct the hypotensive state following removal

The danger of these cases is during the operation, if the patient survives the pressor syndrome he is cured and the prognosis is good because 90 per cent or over of these tumors are benign.

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SYNERGISTIC EFFECTS OF POLYMYXIN B AND TERRAMYCIN ON BACTERIA ENCOUNTERED IN URINARY TRACT INFECTIONS

ERWIN NETER, ELIZABETH H KUNZ, BA AND ELEANOR D MORGAN

From the Laboratory of Bacteriology of the Roswell Park Memorial Institute and the Department of Bacteriology and Immunology, University of Buffalo, School of Medicine, Buffalo, N Y

Attempts to improve the results obtained in the treatment of infectious diseases by the concurrent use of two anti-infectives were undertaken already decades ago, as, for example, in the treatment of syphilis with arsenicals and bismuth or mercury compounds. However, it has been established that the simultaneous use of two chemotherapeutic agents does not always result in synergistic effects. In fact, in some instances, two such compounds may interfere with each other. It becomes necessary, therefore, to investigate both *in vitro* and *in vivo* any contemplated combination of chemotherapeutic agents, in order to determine whether synergistic, antagonistic or additive effects are obtained.^{1 2 3 4} Polymyxin is one of the most powerful antibiotics available against gram-negative bacilli. Its clinical usefulness, however, is limited because of its toxicity, which makes it necessary to limit its use in man to a short period of time and to relatively small doses. In order to determine *in vitro* whether sub-effective doses of this antibiotic may be bacteriostatic or bactericidal when used concurrently with sub-effective doses of another antibiotic, the studies reported in this communication were undertaken. The data obtained indicate that polymyxin B and terramycin act synergistically on various gram-negative bacilli encountered in urinary tract infections and suggest a clinical trial of combined treatment in otherwise refractory cases.

MATERIAL AND METHODS

Polymyxin B sulfate ("Aerosporin") was obtained from Burroughs Wellcome & Co through the courtesy of Dr D S Searle, and terramycin from Chas Pfizer & Co through the kindness of Dr Elliott R Weyer. Stock solutions were prepared in distilled water and stored in the refrigerator. Suitable dilutions were then made in brain heart infusion broth prior to each experiment.

A variety of strains of gram-negative bacilli isolated from patients suffering from infections of the urinary tract were used as test organisms. The microorganisms were grown in brain heart infusion broth for 24 hours at 37C. A 1 to 10,000 dilution of the broth culture was then prepared and 0.05 ml of this dilution was seeded into 2 ml of broth containing various amounts of either polymyxin B, or terramycin, or a combination of these two antibiotics. Broth without anti-

¹ Bachman, M C. *In vitro* studies on possible synergistic action between penicillin and bacitracin. J Clin Investigat, 28: 864, 1949.

² Lankford, C E, and Lacy, H. *In vitro* response of staphylococcus to aureomycin, streptomycin and penicillin. Texas Rep Biol Med, 7: 111, 1949.

³ Klein, M and Kimmelman, L J. The correlation between the inhibition of drug resistance and synergism in streptomycin and penicillin. J Bact, 54: 367, 1947.

⁴ Spicer, S. Bacteriologic studies of the newer antibiotics. Effect of combined drugs on microorganisms. J Lab Clin Med, 36: 183, 1950.

to be performed on the underlying organs with a maximum of safety to the patient and comfort for the surgeon. This approach is accurately and completely described in the original publication. See figures 1, 2 and 3.

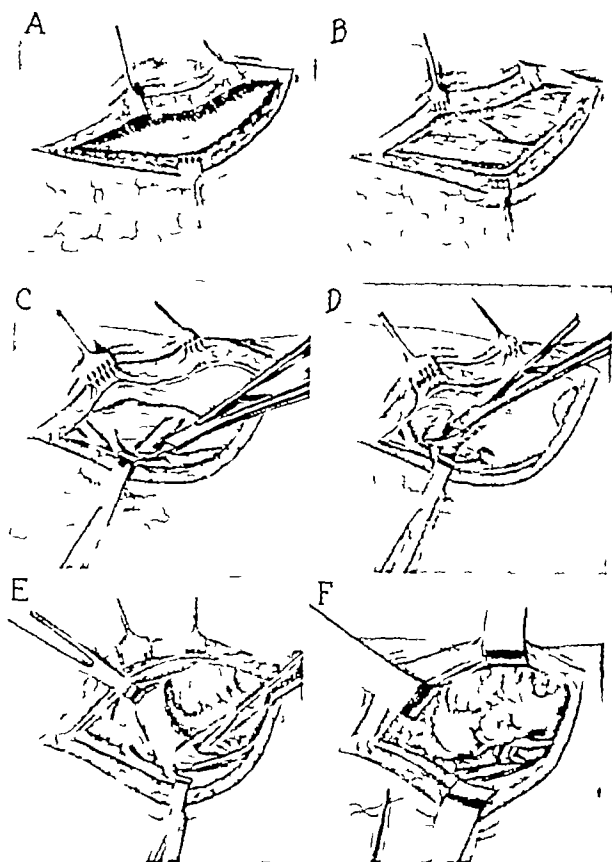


FIG 1 Details of technique. Patient in left lateral decubitus, right kidney incision. *A*, latissimus muscle exposed for division. *B*, serratus muscle ready for division. *C*, twelfth rib segment being removed subperiosteally close to spine. *D*, similar maneuver performed on eleventh rib. *E*, after costal arch has been divided and thorax retracted upward. *F*, lateral arcuate ligament divided below pleural reflection, kidney exposed widely.

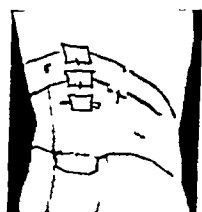


FIG 2 Typical healed incision 2 weeks postoperative. Landmarks pointed on skin.

The previous paper was based on anatomical studies on the cadaver and the clinical application to some thirty untabulated cases. The purpose of this report is to analyze our experience with this approach in an intensive series of 11 cases.

required for growth inhibition after prolonged incubation was due to loss of activity and not due to the emergence of terramycin-resistant mutants. First, it was shown that terramycin in suitable dilutions (ranging from 1.5 to 100 μ g per ml) incubated for 5 days in the absence of micro-organisms was far less effective than freshly prepared dilutions. Second, the organisms growing in the presence of relative large concentrations of terramycin after prolonged incubation proved to be as susceptible to the antibiotic as the parent strain.

A number of experiments were carried out to determine whether the synergistic action of terramycin and polymyxin B results also in increased bactericidal effects. To this end, subcultures were prepared from broths containing either terramycin or polymyxin B or both antibiotics in bacteriostatic concentrations. Repeated experiments showed that death of the organisms occurred in the presence of smaller concentrations of both antibiotics in combination than in the presence of larger concentrations of either polymyxin B or terramycin.

These experiments, then, show that against certain micro-organisms frequently encountered in infections of the urinary tract polymyxin B and terramycin act synergistically. The possibility presents itself of treating patients suffering from such infections which are refractory to commonly used antibiotics and sulfonamides. Such a regime may make it possible to use smaller amounts of polymyxin B than would be required if this antibiotic were used alone and thus may further lessen the danger of side-effects from the use of this antibiotic.

SUMMARY

Polymyxin B and terramycin act synergistically *in vitro* against various bacteria encountered frequently in infections of the urinary tract. This synergism is manifested by increased bacteriostatic and bactericidal effects. This synergistic action is more marked with *E. coli* and *A. aerogenes* than with *P. aeruginosa*, *P. morganii* and *Paracolobactrum*.

The clinical application of combined treatment of refractory cases of urinary tract infection with both antibiotics presents itself.

cation for each case is set forth in table 1 to show the wide range of usefulness of the dorsolumbar flap incision. It is noted that practically every operation and condition encountered in upper urological surgery are covered in this series. Table 1 is discussed in detail below, noting the flexible variations in technique advantageously applied to the particular surgical problem attacked. The discussion is strictly limited to the subject of exposure.

KIDNEY SURGERY

Secondary and tertiary operations on the kidney for calculous or inflammatory disease are notable for the difficulties that they may present owing to insufficient

TABLE 1

PROCEDURE	NO OF CASES
Nephrolithotomy (10 cases)	
Primary	1
Secondary	6
Tertiary	3
Heminephrectomy (2 cases)	
Calculous hydrocalyx	1
Calyceal diverticulum	1
Nephrectomy (17 cases)	
Carcinoma	6
Cyst	1
Calculous pyonephrosis	5
Atrophic pyelonephritis with hypertension (1 with simultaneous sympathectomy)	2
Hydronephrosis	3
Retroperitoneal Exploration (6 cases)	
Nodal dissection for testis tumor	1
Pancreatic duct ectasia	1
Hodgkins granuloma	1
Bilateral Simultaneous Lumbar Exposure (9 cases)	
Adrenal exploration for tumor	1
Bilateral renal calculi	1
Bilateral nephrostomies	1
Total cases	44

exposure. The value of the dorsolumbar flap incision in this group of cases lies in the fact that the incision extends down through relatively normal anatomical structures, skirting previously operated and scarred tissues and reducing the hazard of injury to important contiguous structures. Primary ligation of bleeding points and repair of any injury to other structures under direct vision are added factors of safety for the patient.

In that group of cases in which nephrectomy is wasteful of salvageable kidney tissue, where more conservative procedures such as heminephrectomy, calycectomy, or kidney bisection for staghorn calculus is the more desired solution, careful execution of the surgical technique so essential to success is not possible in many instances due to limited exposure. That extra amount of exposure affor

CARCINOMA OF THE BLADDER Charles P Mathé, San Francisco, Calif

DISCUSSION Gilbert Thomas, Santa Monica, Calif , Jay J Crane, Los Angeles, Calif
RHABDOMYOSARCOMA OF THE BLADDER Herman I Riddell and (by invitation) Howard
Kudish, Los Angeles, Calif

DISCUSSION Frederick Schlumberger, Beverly Hills, Calif , Dean Parker, Seattle, Wash

MAY 22

LYMPHANGIOMA OF THE URETER F B Jeppesen, Boise, Idaho

DISCUSSION Ole Jensen, Jr , Seattle, Wash , Frederick Bennetts, Los Angeles, Calif

FACILITATION OF PASSAGE AND EXTRACTION OF URETERAL CALCULI Earl F Nation, Pisadena, Calif

DISCUSSION James May, San Diego, Calif , Barney Silver, Los Angeles, Calif

JOSEPH F MCCARTHY PRIZE ESSAY AUTOGENOUS VEINS GRAFTS AND VENOUS VALVES IN
URETERAL SURGERY Milton L Rosenberg (by invitation) and Gregory A Dahlen
(by invitation) Stanford University School of Medicine, San Francisco, Calif

LEAKAGE AND REFLUX IN URETERO INTESTINAL ANASTOMOSIS (1) THE FREE PERITONEAL
GRAFT Frank Hinman, Jr , San Francisco, Calif

REIMPLANTATION OF URETERS INTO THE BOWEL Carl K Pearlman, Santa Ana, Calif

CONTROL OF VESICAL NEOPLASM BY DEVIATION OF THE URINARY STREAM, AN EXPERIMENTAL
ANIMAL STUDY Donald F McDonald, Seattle, Wash

A STUDY OF HYDRODYNAMICS OF THE UPPER URINARY TRACT FOLLOWING URETEROSIG-
MOIDOSTOMY Carl F Rusche, Hollywood, Calif , and Wells C Cook, Los Angeles, Calif

DISCUSSION John Hand, Portland, Ore , William Sumner, San Francisco, Calif , Ralph
Mullenix, San Diego, Calif

MAY 22

TRANSPERITONEAL APPROACH TO LESIONS OF THE LOWER URETER John W Schulte, San
Francisco, Calif and (by invitation) Bernard R Sears, San Francisco, Calif

DISCUSSION H V Findlay, Santa Barbara, Calif , Raymond Tyvand, Seattle, Wash

NEPHROCOLONIC FISTULA A DUAL CASE STUDY Milo Ellik, Long Beach, Calif and (by in-
vitation) John Getz, Torrance, Calif

DISCUSSION A J Scholl, Los Angeles, Calif , Ector LeDuc, San Diego, Calif

REPORT OF A CONTROL CASE OF NEPHROPTOSIS IN A PAIR OF IDENTICAL TWINS Carl E
Ebert Los Angeles, Calif

DISCUSSION Walter Pritchard, San Bernardino, Calif , Wilbur Rogers, Glendale, Calif
CLINICAL CONSIDERATIONS IN APLASIA, HYPOPLASIA AND ATROPHY OF THE KIDNEY Carl
E Burkland, Sacramento, Calif

DISCUSSION Allan Howard, Los Angeles, Calif , William Carroll, San Francisco, Calif
PAINFUL PERIPELVIC RENAL CYST Samuel Peck, San Diego, Calif

CALICEAL DIVERTICULA OR PYELOGENIC CYSTS Rollin G Wyrens, Seattle, Wash

DISCUSSION Tracy Powell, Los Angeles, Calif , C Balcom Moore, Walla Walla, Wash

PAPILLARY TUMOR OF THE KIDNEY PELVIS WITH MULTIPLE URETHRAL TRANSPLANTS Philip
B Potampa Portland, Ore

DISCUSSION Morrell Veckl, San Francisco Calif , Davis Pardoll, San Bernardino,
Calif

this exploration may be felt in that exposure of that entire area may not be possible through one approach. Here the dorsolumbar flap incision may be used unilaterally or bilaterally depending on whether or not the opposite adrenal must be visualized. If unilateral exploration has been decided upon, the patient is placed in the lateral decubitus position and the lateral tilt of the operating table may be adjusted so that the patient is canted some 15 degree anteriorly away from the operating surgeon. In this manner, all the retroperitoneal structures, and the spleen, pancreas body and tail, and the colon flexure (on the left side) may be visualized in one operative field. The posterior parietal peritonum may be safely opened if biopsy or surgery on these latter organs is desired.

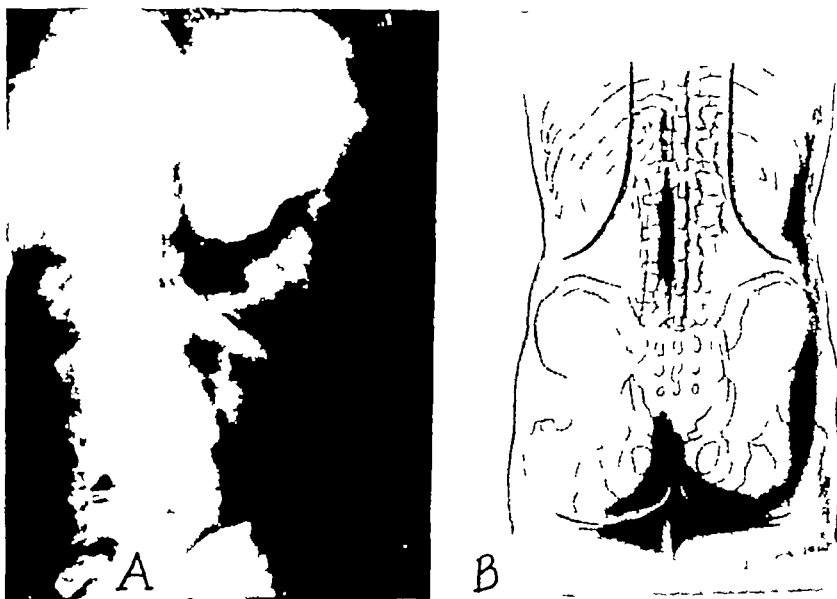


FIG. 4. A, perirenal insufflation showing mass on left side, adrenal disease suspected clinically. B, diagram showing placement of skin incisions for bilateral dorsolumbar flap incisions.

BILATERAL SIMULTANEOUS LUMBAR EXPOSURE

The dorsolumbar flap incision is admirably suited for adequate bilateral simultaneous exposure of the adrenal glands (figs. 4 and 5). The most practicable way to look at both adrenals at the same time is to place the patient in the prone position in the manner described by Young.² In the surgical treatment of adrenal hyperplasia particularly, where complete extirpation of one gland and possibly as much as 80 per cent resection of the other gland has been advocated, proper execution of such an exacting procedure requires ready accessibility of the glands for careful evaluation, exactitude in extirpation and resection, and accurate suturing. All this must be performed with the minimum of handling and traction. The Young incision is not adequate in achieving this accessibility in many cases.

² Young, H. H. *Genital Abnormalities, Hermaphroditism and Related Adrenal Disorders*. Baltimore: Williams & Wilkins, 1937.

PHEOCHROMOCYTOMA DIAGNOSIS AND TREATMENT

GEORGE F CAHILL

*From the J Bentley Squier Urological Clinic, Columbia-Presbyterian Medical Center,
New York, N.Y.*

For an unusual and infrequent tumor, pheochromocytoma has received considerable attention and there still seems to be a lack of agreement upon the various tests used in establishing a diagnosis, and because of their variations a diagnosis is at times difficult. The tumor occurs with sufficient frequency so that its presence should always be suspected in any hypertensive having either vasomotor attacks or hypermetabolism or both symptoms. Only by having a suspicion of the presence of the tumor and a proper evaluation of the case will the correct diagnosis be made. Because many more cases are suspected of the tumor and proven to be without its presence, there should be no deterrent to still seek its presence in such suspected cases because if found its correction by surgical procedure will produce a cure.

The symptoms and signs of pheochromocytoma rarely depend upon pressure effects or displacement of an organ, but depend upon the secretion by the tumor of hormone or hormones with many and varied actions. It has been shown that the tumors produce at least two active substances, epinephrine and nor-epinephrine in various amounts, and that the symptoms produced are assumed to be the result of an excess of varying amounts of these two active substances. As yet it is not clear just how the various fractions of these substances or perhaps some as yet unidentified substances produce all of the variables in the symptoms seen. Also it has been shown that some of these tumors rarely in the abdomen and chest do not produce any symptoms at all. This has been especially true of the tumors of the same tissue in the carotid body.

Tumors have been found under the following conditions

- 1) An individual, symptom-free, in whom a tumor has been found on accidental examination or at autopsy
- 2) An individual with a sudden hypertensive attack, or sudden death following a minor or a major trauma, at times a surgical operation, and the tumor then discovered at operation or later at autopsy
- 3) The adrenal sympathetic syndrome
 - a) With a usual normal blood pressure with intervals of paroxysmal hypertension
 - b) More or less continuous hypertension with paroxysmal rises
 - c) Constant hypertension simulating essential hypertension

Since discussion for diagnostic purposes involves the adrenal sympathetic syndromes, these only will be considered. From the reported cases the following items may be stated. The tumors occur most frequently in adult females, next in adult males and less often in children of both sexes. The tumors may be single or multiple, often two have been present, very rarely more. Multiples occur in 10 per cent of the cases. The tumors are most frequent in the adrenal medulla next in

Read at annual meeting Western Section, American Urological Association, Sun Valley, Idaho June 26 1951

symptom with typical distribution of the fat in huge pads at the waist and shoulder girdles, the patient weighing 210 pounds of which 100 pounds had been gained in the past 6 months. Operation was advised when first seen but refused. When the family realized that there was no alternative but operation, the cardiac status was such that the patient presented a serious surgical risk. Bilateral simultaneous adrenal exploration was performed. The extreme obesity in a short-waisted boy of nine and the problem of maintaining unimpeded abdominal breathing in the prone posture made the operation very difficult technically. One adrenal was hypoplastic and the other hyperplastic illustrating the importance of bilateral simultaneous visualization. The hypoplastic adrenal was completely removed and the hyperplastic gland subtotally resected. The patient did not react from postoperative shock and died with attendant cardiac failure.

There was one wound infection in this series, occurring in a case of retroperitoneal unilateral exploration for a mass demonstrated by preoperative roentgenographic study. A large mass was found in the depths of the wound in relationship to the adrenal, kidney, spleen and colon, all of which were found to be normal. Frozen section biopsy of the mass returned the diagnosis of pancreatic duct ectasia, and the wound was closed around a Penrose drain without further surgery. On the fourth postoperative day a thick creamy discharge containing amylase and lipase was noted from the drain site and pancreatic enzymic digestion was suspected. However, laboratory culture demonstrated the presence of wound infection which was treated and progressively eliminated without sequelae.

Inasmuch as the dorsolumbar flap incision is an extrapleural technique in which the pleural cavity is not deliberately traversed, a pleural tear during the operation while not serious is to be considered an accident. We had three such accidents in our present series. When one is working so close to the pleura, this possibility must be anticipated, and endotracheal anesthesia is recommended as a routine. As our experience progressed we learned how to minimize the possibility of tears. In the original and present series, pleural tear did not occur during the segmental rib resection or from the cut end of the rib. In the first few cases where we tried to dissect the pleura off the diaphragm, we found that this was not technically feasible enough to be of practical value. Thus by locating and dividing the lateral arcuate ligament of the diaphragm at its attachment to the quadratus lumborum muscle, the diaphragm is wiped upward with its continued intact pleural reflection (the costophrenic sinus). If this is performed with care and deliberation, it is entirely possible to avoid pleural injury. If further exposure is necessary in the deeper reaches of the wound, a similar maneuver is carried out with the medial arcuate ligament of the diaphragm where it attaches to the psoas major muscle.

A pleural tear is most likely to occur at the posterior extremity of the incision, where the now mobile diaphragmatic pleura is reflected onto the fixed parietal pleura. If the upper portion of the costovertebral ligament must be divided in this region, it should be carefully divided as close to the spine as possible. Retraction at the posterior angle unprotected by a lip pad, uncontrolled retraction, or the undivided and unnecessary attempted dissection of the parietal pleura or the chest wall are other factors which invite pleural damage.

subjected to lumbar dorsal sympathectomy With persistent hypertension and tumor, several other manifestations are often present which should lead to the suspicion of tumor Most of all the tumor cases have hypermetabolism, shown by elevated basal metabolism rate Most are subject to easy and marked sweating Rapid pulse and mild elevation of temperature and some leukocytosis are often present Glycosuria and elevated blood sugars may be present but are more often accidentally associated with hypertension without any tumor being present Whether the persistent hypertension is due entirely to the relative amounts of epinephrine and nor-epinephrine or their secretion in a continuous amount or are due to other hypertensive factors is as yet not clear, but in most cases it seems to be due to their presence Within the persistent hypertensions that have been treated as hypertensives, probably lay the larger numbers of unrecognized pheochromocytomas Since the finding of a tumor may result in a cure, any hypertensive with other suggestive symptoms should be suspected and investigated for the presence of a tumor

PHARMACOLOGICAL TESTS

For the purpose of diagnosis, when persons appear with symptoms suggestive of pheochromocytoma, various pharmacological tests have been devised to show the presence of excess pressor substances in the blood The classical chemical analysis by Ernold and Picaral in 1934 and the pharmacological demonstration by Beer et al in 1937 have not subsequently appeared in the literature as having been used The tests reported have been divided into the use of epinephrine and nor-epinephrine provocatives and the use of epinephrine and nor-epinephrine antagonists The attacks of hypertension in tumor have been brought about by many causative factors—emotions, fear, anger, change of posture, trauma, massage of the tumor if palpable, cold pressor tests or the direct use of chemicals

PROVOCATIVE

Roth and Kvale⁴ suggested and used the intravenous injection of 0.05 of histamine base They showed that with a tumor after a very short initial drop in blood pressure there is a marked rise associated with symptoms of precordial and abdominal pain, headache, nausea and marked sweating The duration of the crisis was short and the blood pressure returned to near its former level Repetition produced similar results They recommended that the patient should not have any sedation 12 hours previous to the test

The test when properly performed has been quite reliable when tumor is present and its value has been repeatedly confirmed It has been reported as negative in cases by Aranow, Jr.⁵ and by Calkins et al.⁶, as yet without clear explanations This compared with the large number in which tumor has been confirmed has established a high positive accuracy for tumor However, other hypertensives have reactions suggestive of those seen with tumor and no tumor found In

⁴ Roth, G. M. and Kvale, W. F. *Am J Med Sc*, 213: 324, 1947

⁵ Aranow, H. Jr. *Med Clin North Amer*, 34: 757, 1950

⁶ Calkins, E., Dana, G. W. and Howard, J. E. *J A M A*, 145: 880, 1951

DISCUSSION

DR RICHARD CHUTE (Boston, Mass) I wish to compliment Dr Nagamatsu on his well-thought-out and ingenious incision I have used it, and it gives excellent exposure of the kidney and of the infradiaphragmatic region, and has the advantage of staying out of the pleural cavity Possibly because I have been one of the advocates of the use of the thoraco-abdominal incision for the same purposes, I still prefer that approach except not for bilateral simultaneous operations In the Nagamatsu incision, the diaphragm and pleural cavity are swung up out of the way, like lifting the cover of a hinged box, where as in the thoraco-abdominal the approach is made simply and directly through the diaphragm right down on top of the adrenal and kidney, giving a somewhat wider exposure than the Nagamatsu, especially for the removal of malignant nodes located high up on the vena cava and aorta in the region of the central portion of the diaphragm Also any local extension to the diaphragm can be resected The Nagamatsu incision is slower and more difficult to make, as parts of 2 or 3 ribs have to be removed, and great care and gentleness must be exercised to avoid entering the pleural cavity, and if this is entered, then the whole point of this somewhat complicated technical procedure is lost Be that as it may, I wish to compliment Dr Nagamatsu on his excellent approach which shows much thought and originality, and which I am sure will be widely used by urologists, especially those who feel quibbles about deliberately entering the pleural cavity

Any contribution of Dr Foley's commands respect—and his associates' paper today is no exception * He is doing surgeons a great service by not only calling attention to and proving the importance of removing the perinephric fat intact inside its capsule in cases of hypernephroma, but also in describing the technique of exactly how this is done I agree wholeheartedly with this and—as a matter of fact—I and several of my colleagues have been separating the peritoneum from the renal or Gerota's fascia, and removing the perinephric fat intact inside its fascial capsule and en bloc with the kidney—just as described by Dr Foley—for several years now, and I imagine that many surgeons have been doing the same

However, I am sure that there must also be many surgeons who are not doing this, partly because they have not realized the importance of so doing, and partly because just how to go about it has not been called to their attention

In view of the pathological findings of Drs Beare and McDonald that 70 per cent of nearly 500 cases of hypernephroma had involvement of the fibrous capsule of the kidney, usually with extension of the disease into the perinephric fat, it becomes apparent that it is definitely poor surgery in cases of cancer not to remove the intact perinephric fat en bloc with the kidney

In agreement with the trend of malignant extension reported by Beare and McDonald are my own observations in a series of 38 renal tumors—mostly hypernephromas—operated upon by my colleagues and myself through the

*The paper by Drs Foley, Mulvaney, Richardson and Victor will appear in a later issue Editor

in our hands, no tumor has been found. From collected reports it appears as if a positive response has always been associated with tumor, and thus also has been the result of our experience.

These pharmacological tests so far have been helpful in establishing the presence of tumor. They however have to be evaluated with the other symptoms and signs and then usually a diagnosis may be established.

RADIOGRAPHY

The visualization of a tumor is a very important diagnostic procedure in these chromaffin tumors. With a large tumor a shadow may be present upon a plain abdominal film and at times calcification may be present in a tumor and bring out its shadow. Pyelography has shown displacement of the kidney downwards by the tumor mass and in some a flattening of the upper pole of the kidney may occur. Similar shadows have been shown to occur by other organs, as we have recently seen a retroperitoneal normal spleen produce these changes. In 18 cases in a collected report by Howard and Barker,¹² 11 had the tumor diagnosed by pyelography. Perirenal insufflation has enabled us to establish the diagnosis when the tumor is within the adrenal. The use of gas insufflation in the localization of small tumors of the adrenal must be stressed because often the site of such cannot be identified by any other method. When the tumor is without the adrenal there may be difficulty in outlining it with gas and of course difficulty in recognizing its situation. In one, a lower right ganglion tumor, we were able to show the tumor well with gas insufflation. In several cases in which the tumors were near the aorta and the tumors under pressure, the failure of the gas to infiltrate through the fascial planes suggested the site of the tumor. In fact, in reviewing the films after removal of the tumor or tumors the outlines were then clearly distinguishable. The infiltration of the gas often gives a lead in its physical outlining but experience in their interpretation takes time. Laminographic x-rays have also successively shown these tumors, especially when used with gas insufflation. The abnormal presence of other organs with laminograms may make confusing films as recently seen with an abnormally situated pancreas above a left kidney. Aortography, first used for showing an adrenal tumor, has been used by ourselves and others but its value has as yet not been clearly established. When a tumor is intrathoracic the tumors have been clearly seen, as reported by Phillips,¹³ Maier¹⁴ and Humphreys.¹⁵ Here the lungs conveniently supply the contrasting air and the smooth outlines of these tumors have been clearly shown. Because of the possibility of intrathoracic tumor, all cases of suspected pheochromocytoma should have such investigative films.

TREATMENT

The treatment of pheochromocytoma is surgical removal of the tumor or tumors if more than one is present. It has been shown that surgical removal of

¹² Howard, J. E. and Barker, W. H. *Bull. Johns Hop. Hosp.*, 61, 37, 1937.

¹³ Phillips, B. *Arch. Path.*, 30, 916, 1940.

¹⁴ Maier, H. C. *Ann. Surg.*, 130, 1059, 1949.

¹⁵ Humphreys, G. H. 2nd. Personal communication.

lived he was essentially anuric, so it seems probable that the left renal vein was occluded by the ligature. The two other cases in which the vein was ligated and a section of it removed for tumor involvement, both had worrisome immediate postoperative courses with marked oliguria for a week and great elevation of the nonprotein nitrogen of the blood, but they eventually made satisfactory convalescences. One of them had considerable edema of the legs for 6 months.

Now, for the performance of this somewhat exacting surgery, the surgeon needs a truly wide exposure. Although I bow to Dr. Foley's surgical skill, I don't see how beginners or those of us who are less adroit than he can get an exposure really wide enough through the incision which he uses, apparently a glorified lumbar incision. Therefore, when dealing with renal tumors, I would strongly recommend the thoraco-abdominal incision or the Nagamatsu incision or the type devised by Dr. Sweetser. The extra trouble taken in making and closing these incisions is made well worth while by the ease and safety with which difficult situations can be handled through them.

Although I have differed somewhat from some of the views expressed by Dr. Foley, *this is an honest difference of opinion with a friend whom I admire*. Foley has made many important contributions to urology, such as the universally used Foley catheter and the Y plasty for ureteropelvic obstructions, to mention only two.

And now in this paper Dr. Foley and his associates are performing a great service to surgeons, as well as to countless future patients, by stressing the modern radical approach for surgery of renal cancer.

DR. THEODORE H. SWEETSER (Minneapolis, Minn.) Any good surgery requires adequate exposure. Dr. Nagamatsu's incision, in my experience, has given wonderfully good exposure for extensive and accurate work in that region. Perhaps I have been too conservative, but I have thus far felt that the classical flank incision has been adequate for most cases and have reserved his more extensive incision for patients in whom the diagnosis of renal malignancy seemed fairly certain. I have found it easier and less time-consuming than the incision which I described before this body in 1946. With further experience I expect to use it more frequently and for a wider variety of cases.

Dr. Foley's approach is also sound and I agree with him that in cases of renal tumor the renal pedicle must be reached before disturbing the kidney, and that all the perirenal fat and renal fascia must be removed with the kidney. I know from experience that such is possible also by the incision I described and by Dr. Nagamatsu's approach. I was glad to note that Dr. Nagamatsu recognized that the interior part of his incision may be extended across the rectus muscle to the midline if necessary to gain perfect freedom in exposing the renal pedicle. The diagram (slide) accompanying my paper in 1946 clearly shows that I followed the line of cleavage outside the renal fascia as described by Dr. Foley but I will admit that in one of the other drawings (slide) the perirenal fat was removed to show the pedicle more clearly.

Both operations presented today are basically sound, and are good surgery in the present state of our knowledge. We all hope for the day when someone

peutic and in 3 cases of pheochromocytoma. He states that it has apparently produced a more pronounced and more prolonged reduction in the blood pressure when used for diagnosis than did benzodioxane in the same cases and in its therapeutic effect it was more effective, more easily controlled and less toxic than dibenamine. He used it in varying amounts in each patient, 0.08, 0.16 and 0.3 mg. of regitine per kilo intravenously 2 hours before operation. It was necessary during the handling of the tumor to give two subsequent injections of 0.16 mg. to prevent a beginning rise. He believes that regitine with benzodioxane will be the two drugs to use. Further experiments with this drug are necessary to confirm these observations.

With small tumors and in patients in good condition it is not as yet decided that these sympathicolytic drugs are necessary if complete blood vessel severance is done before the tumor is manipulated. The marked hypertensive rise is then avoided. Moreover, with the patient free from the inhibitory effects of these drugs the sustaining hormones introduced after the removal of the tumor usually have a prompt effect.

The anesthetic problem in these cases has been largely concerned with four important elements, adequate relaxation, the possibility of pneumothorax, the physiological effect of excessive secretion of epinephrine or nor-epinephrine during the removal of the tumor and the sudden circulatory depression which may occur after extirpation of the secreting mass. From the literature, all types of premedication and anesthetic agents have been used. No matter what anesthetic regimen is followed anoxia must be avoided. Anoxia appears to be as potent a stimulus to medullary secretion as tumor manipulation. Agents which, in the presence of epinephrine produce serious ventricular arrhythmias must be avoided, cyclopropane, chloroform and ethyl chloride are therefore unwise choices for anesthesia. The marked hypotension and circulatory collapse after excision of the tumor has been best controlled by the injection of an intravenous drip of nor-epinephrine (4 mg./liter). The drip is usually given at a rate which will maintain moderate hypertension. It is an essential therapeutic aid in the first 3 days of postoperative convalescence. The anesthetic agent most often used by us has been basal avertin and ether and oxygen.

These tumors have been removed surgically by all routes, flank extraperitoneal incisions with or without rib resection. Thoracic abdominal incisions are now enjoying a vogue as well as rib resection flap extraperitoneal incisions. Because of the multiplicity of these tumors and because of the variability of their locations, the transverse upper transperitoneal abdominal incision has appealed to us as offering the best approach. Experience with these tumors has in our hands shown this apparently to be superior to others. The value of an adequate exposure is obvious and if possible the blood supply to and from the tumor should be occluded before manipulation of the tumor. In the large tumors on the right side close to the vena cava this is often difficult and occlusion clamps may be needed for the cava above and below the tumor before the vessels are ligated. With the adrenolytic agents in the large tumors the former dramatic fluctuations of blood pressure seen in handling of the blood vessels have been lessened. After

consider making the oblique part of his incision first. With such slight modification I believe that both operations are safe and basically sound surgical procedures.

DR N. Y. BAKKER (The Hague, Holland) I first wish to compliment Dr Nagamatsu on his fine paper, in which he showed us the advantages of his incision, and which certainly is a much better exposure than the resection of the twelfth rib only, which is routinely done in our country.

One indication for his incision seems to be node dissection in testicular tumor, and this is where I want to come in. As my friend, Dr van Gulik, and I came to this country, we were very anxious to learn of new methods of investigation, new drugs and new operative techniques, meaning to bring those which seemed useful to us home to Holland.

One of the new techniques we heard so much about here, and which we saw performed in several hospitals, was the radical operation which you do in this country for malignant tumors of the urogenital tract. In fact, we got the impression that these operations are the natural thing to do here when you encounter a neoplasm in this field of surgery. This is certainly not so on the Continent, as far as I know.

I can tell you that I admired very much the beautiful movies you showed us of these procedures, and the skill with which these operations are performed.

The question now arises, if we are to bring these operative techniques with us to Holland, can anyone here in this convention tell me what the real and true value is of these (in most cases) formidable procedures? Do you believe, for example, that when you find, in a case of malignant testicular tumor, nodes in the region of the renal pedicle, and you remove these, that the patient will have a longer life expectancy? Don't you think that there will be many more metastases higher up, or on the other side, which you leave behind, and which will kill the patient in as short a time as without the operation? And aren't you afraid that in handling these glands and dissecting them, you will displace malignant cells, which will take root in another region of the body?

Of course, you will say, "Don't you remove the axillary glands in a case of carcinoma of the female breast?" Of course we do. But what are the results? As far as I know, they are not so good. And in these cases the procedure takes you only some 20 minutes more, whereas I saw performed in this country a cystectomy with node dissection and ureteral anastomosis into the bowel which took 7 hours, and was not yet finished. I can tell you that we in Holland couldn't afford such a long time for one operation only.

You will ask, "Why not?" and I will tell you "Because of socialized medicine." Eighty per cent of the population in The Netherlands is taken care of by socialized medicine. That means that we have to examine and treat, 3 mornings a week, 50 to 60 outdoor patients of socialized medicine alone, part from our private practice and clinical work, and that on such mornings we have to do 6 to 10 cystoscopies, all of this with the help of one assistant and one nurse only. If we would go into the matter of dissecting nodes in all our patients with malignancies of the testicle, prostate, bladder or kidney, it would be quite un-

THE DORSOLUMBAR FLAP INCISION IN UROLOGIC SURGERY

GEORGE R. NAGAMATSU, PHILIP H. LERMAN AND MICHAEL H. BERMAN

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The kidney and adrenal gland are subdiaphragmatic organs, and more often than not are situated high in the retroperitoneal space. It is an experience common to all urologists that, when the pedicle is short and immobile or when the organs are altered by disease, the overhanging bulwark of the lower thoracic cage makes surgical access to this area difficult and often impossible through the usual lumbar incision.

Removal of the twelfth, and on occasion the eleventh rib also, is of great aid in attaining good exposure.¹ However, the extensive and exacting surgical techniques that are the rule of the day, require the maximum of exposure often crossing traditional anatomical barriers. Chute and Soutter² have successfully traversed the pleura and diaphragm and abdomen to expose the upper limits of the retroperitoneal space.

Recognition of the axiom that there is no longer a necessity for the urologist to operate on such vital organs as the kidney and adrenal through an inadequate blind "manhole" type of retroperitoneal incision prompted one of us to develop an extrapleural approach offering wide exposure to this area, the so-called dorso-lumbar flap incision.³

This incision has a dorsal and a lumbar component. The dorsal component is made by a skin incision starting just above the superior border of the angle of the twelfth rib. From this point the incision is carried upward parallel to the lateral border of the sacrospinalis muscle ending at the tenth interspace. After the latissimus and serratus muscles are divided, short segments of the eleventh and twelfth ribs are resected medial to their angles. This completes the bony mobilization of the flap. The lumbar component is a continuation of the dorsal incision and is similar to the conventional lumbar incision extended to the lateral margin of the rectus muscle. To free the flap for upward retraction, the entire costovertebral ligament is divided. This exposes the posterior attachment of the diaphragm to the quadratus muscle. By incising this attachment below the pleural reflection, the diaphragm and its attached pleura (costophrenic sinus) are freed and retracted upward. Thus the entire retroperitoneal space up to the dome of the diaphragm is now completely exposed. A replaceable extrapleural osteoplastic flap has been made that unroofs the lower thoracic overhang and allows surgery

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¹ Hess, C. J. *Urol* 42: 943, 1939.

Chute, R. and Soutter, L. *J Urol* 61: 688-696, 1949.

³ Nagamatsu, G. *J Urol*, 63: 569-577, 1950.

For these common operations, resection of approximately an inch from the twelfth and the eleventh ribs puts the kidney in the lower portion of the wound. No longer does one have to reach up under the ribs to mobilize the kidney or to do any operative manipulation. It is a most astonishing and gratifying sensation to see the kidney in the lower portion of the wound, where it is so easily accessible.

The second group of operations using this technique consists of those cases that require an extensive exposure for renal tumors, adrenal gland disease or retroperitoneal dissection of lymphatics from testis tumors. Here one resects a portion of the lower three ribs, and thereby obtains a completely adequate exposure to the diaphragm.

As does Dr. Foley, we also practice and recommend radical surgery for tumors of the kidney and in my opinion such a radical operation requires ligation of the pedicle before any manipulation of the tumor, removal of the growth with the perinephric fat, dissection of the lymphatics about the aorta and vena cava as high as the diaphragm, and sometimes entering the vena cava for the extraction of a tumor embolus. It must be emphasized that all such operations must be planned in advance, because they must be performed through an adequate approach. The Nagamatsu incision provides it amply.

In recommending the Nagamatsu approach, I do not in any way criticize the thoraco-abdominal approach. We have had a small experience with 15 such incisions for various conditions and have never found it anything but excellent and there have been no postoperative complications of any kind, but, I somewhat differ from Dick Chute in thinking that the Nagamatsu incision takes much less time.

Recently I was delayed because of a thoraco-abdominal operation preceding me, and I found by actual timing that the exposure required one hour and the closure two hours. When I resect a portion of two ribs in doing the Nagamatsu incision, it doesn't lengthen the operating period more than 15 minutes, and, for the resection of three ribs, about 20 minutes.

Another point which hasn't been mentioned in all of this discussion is that for large kidney tumors the Nagamatsu incision can be carried over to the anterior midline of the body and then that limb can be extended cephalad to the sternum. That is similar to the anterior limb of Dr. Sweetser's incision, which, removed from the kidney tumor the shelf on which it lies and causes it to fall forward thus exposing the pedicle very clearly.

Another point in comparing the Nagamatsu and the thoraco-abdominal incisions is that just as urologists prefer not to enter the peritoneal cavity in performing the kidney operations, so, unless it is necessary, we should not enter the thoracic cavity.

DR. GEORGE R. NAGAMATSU. I will take just a minute to thank all the people who took part in the discussion, because I think we are all working toward the same thing, namely, adequate exposure and consequently skillful and adequate surgery in an area of the body which is difficult of access.

Our residents are taught every known procedure in the book. Dr. DeMeer

operated at the above mentioned institutions in the 6 months period from November 1950, to April 1951. In our hands the exposure was found to be adequate in every instance in this series.

The dorsolumbar flap incision was not used routinely for all cases that came to our services, and certainly we do not advocate its use where the usual lumbar approach will suffice. However, as one becomes more and more familiar with its execution and realizes its safety and simplicity, the tendency is to use it for an ever increasing variety of indications. These indications are:

1) Kidney surgery requiring wide exposure, as in tumors, high-lying kidneys, secondary and tertiary operations, heminephrectomy, calycectomy, and in general, whenever the preoperative evaluation appears to present an exposure problem.



FIG 3. Postoperative film illustrating normal realignment of ribs and lower thorax after dorsolumbar flap has been replaced.

2) Adrenal surgery, especially bilateral simultaneous exposure, where the lesion cannot be lateralized preoperatively and visualization of both adrenals must be adequate before surgery can be performed on either.

3) Retroperitoneal gland dissection for testis tumor, where the en-bloc dissections must begin in the subdiaphragmatic and suprapedicle zones.^{4 5}

4) Bilateral kidney surgery, such as bilateral nephrostomy or bilateral nephrolithotomy.

5) Thoracolumbar sympathectomy combined with nephrectomy (in selected cases).

The surgical procedures performed on these 44 cases and the individual indi-

⁴ Lewis, L. J. *Urol*, 59: 763, 1948.

⁵ Cooper, J. F., Leadbetter, W. F. and Chute, R. *Surg, Gynec & Obst*, 90: 486-496, 1950.

NEPHRO-URETERECTOMY A NEW TECHNIQUE

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AND CLINTON E STURDEVANT

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Complete ureterectomy, in addition to removal of the kidney, is indicated in patients with papillary carcinoma of the renal pelvis and in many patients with marked ureterectasis. A new technique for this operation is presented.

Removal of the entire ureter prevents transplants of tumor from the renal pelvis to the lower ureter and to the ureteral orifice. Such a transplant of papillary carcinoma from the renal pelvis to the ureteral orifice and stump of the ureter was responsible for our developing the technique presented here today.

In 1948 we performed a nephrectomy upon a patient with papillary carcinoma of the renal pelvis. The ureter was entirely normal in appearance and only the upper two-thirds was removed with the kidney. A year later the patient came back with hematuria. Cystoscopic investigation revealed a papillary mass obscuring the ureteral orifice. This mass with the surrounding portion of the bladder was resected transurethraally with the McCarthy resectoscope using a special short beaked sheath. The opening of the ureter was then seen in the fossa of the resected area, it was entirely disconnected from the bladder. A ureterogram was obtained by catheterizing this opening and injecting contrast medium, this showed that the entire stump contained carcinoma. Immediate removal of this ureteral stump was done through midline abdominal incision. Upon exposing the ureteral stump it was easily delivered, the lower end having been disconnected from the bladder greatly facilitated the procedure. No attempt was made to close the opening in the bladder. A Penrose drain was placed through stab wound into the ureteral bed. A balloon type retention catheter was left in the bladder for fourteen days and upon its removal the bladder was healed.

In patients who require nephrectomy for reasons other than carcinoma and who exhibit ureterectasis, particularly of the lower third of the ureter, it is important to remove the entire ureter. To do so prevents later abscess of the ureteral stump and removes a possible source of continued infection. See figure 1.

The usual procedure for removal of the entire ureter along with the kidney requires two incisions or at least extension of the kidney incision almost to the pubis. Also it has been found at times difficult to remove the intramural portion of the ureter so that in some instances this part may be left.

If the ureter is first disconnected from the bladder by transurethral resection of the ureteral orifice, operation of nephro-ureterectomy can be easily and simply performed. The additional incision in the lower abdomen is not needed and therefore the time of operation is shortened. This new technique has been used by us on six patients with uniformly satisfactory results.

The technique consists of two parts, transurethral and open. Using the Mc

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ded by the dorsolumbar flap incision often makes possible the kidney-sparing operation rather than the easier compromise of a nephrectomy. Such was our experience in 2 cases in this series.

In the handling of tumors of the kidney where direct initial access to the kidney pedicle and excision of contiguous fascial and glandular structures are manifestly desirable, we advocate and practice the routine use of this incision. The kidney pedicle in the majority of cases of this group is most easily approached from the anterior and superior aspect of the renal mass, somewhere in the plane between the anterior axillary line and the lateral margin of the rectus muscle. The dorsal component of our incision frees the anterior ends of the lower ribs in order to allow greater upward freedom to the abdominal component, just where access to the pedicle is possible. Segmental resection of two ribs, which may be the tenth and eleventh if a rudimentary twelfth is bypassed, has been found to give ample bony mobilization. Emphasis is made at this point that an adequate lumbar component is a necessity. In order that this component may be adequate, the incision may be carried across the upper abdomen cutting the rectus muscle with or without an incision through the peritoneum. Dean⁶ has used the modification described by Sweetser⁷ in conjunction with the dorsolumbar flap incision. We have had no experience with this combination but the addition of an anterior vertical leg up to the xiphoid seems logical where further upward freedom is required.

RETROPERITONEAL GLAND DISSECTION FOR TESTIS TUMOR

The dorsolumbar flap incision is readily applicable to retroperitoneal gland dissection for testis tumor. We start our nodal dissection at the dome of the diaphragm and proceed downward in the manner described by Cooper, Leadbetter and Chute.⁴ The kidney being of normal size nominally is retracted downward and forward. The entire space under the diaphragm then presents itself in the wound without recourse to undue retraction and the fascia and nodes in this area may be dissected and removed. By extending the lumbar component of the incision downward obliquely, wide medial retraction of the abdominal flap exposes the great vessels with their accompanying chain of lymph structures for removal in continuity. Vallett⁵ has also used this method of exposure. In the handling of certain tumors of the testis, the magnificent exposure afforded by the dorsolumbar flap incision making possible a satisfactory gland dissection, we have been stimulated to include this radical form of surgery as a part of the regimen.

RETROPERITONEAL EXPLORATION

In those cases where the roentgenographic evidence including pyelography, perirenal insufflation, barium enema, and possibly renal arteriography suggests the presence of a mass in the retroperitoneal space, a certain number must be explored before a definitive diagnosis is possible. Some hesitation in accepting

⁶ Dean A. L. Personal communication.

⁷ Sweetser T. H. J. *Crol.* 57: 651-659, 1947.

⁵ Vallett, B. S. To be published.



FIG. 3 Separation of ureter by traction and dissection



FIG. 4 Balloon type catheter in bladder, stab wound for drainage of lower part of ureteral bed. Lumbar incision closed in usual manner

mainly because the adrenals are buried in the fat under the thoracic shelter. By including the 2-rib-segment dorsolumbar flap maneuver bilaterally with two teams operating, and swinging the lumbar component out toward the flanks, the thoracic cage can be retracted upward and outward and the kidneys retracted downward, bringing the adrenals well into the zone of surgical access. It is important to remove the rib segments as close to the spine as possible and to swing the lumbar component obliquely outward in order to give maximum freedom to the upward flap. It is in this type of surgery where this incision is probably most useful. These wounds heal well unless there is a systemic modifying factor, the postoperative morbidity is no longer than for other incisions of this type, and the postoperative roentgenograms reveal no bony or diaphragm displacements. As a consequence, the movements of the spine are not limited and no disability has been seen.



Fig 5 Wide exposure of large pheochromocytoma in situ

Bilateral simultaneous renal operations are sometimes necessary. Nephrostomies for acute bilateral urinary obstruction is a procedure that must be done as they are encountered from time to time on any active urological service. Bilateral stone disease in the kidneys is safely and advantageously handled at one sitting in certain selected cases. Gibson¹⁰ in a comprehensive article on the problem discusses the indications and the advantages of the bilateral procedure and presents a modification of the Young approach. We also find that the prone position is the best and most practical. If the exposure is cramped in any way, we do not hesitate to apply the dorsolumbar flap technique bilaterally as above described.

RESULTS AND COMPLICATIONS

In this series of 44 cases there was 1 death. This occurred in the case of a 9 year old boy with an adrenogenital syndrome. Marked obesity was a cardinal

¹⁰ Gibson, T. E. J. Urol., 63: 991-996, 1950.

DISCUSSION

DR CHARLES C HIGGINS (Cleveland, O) Ureteronephrectomy or nephro-ureterectomy is a sound surgical procedure based upon well established fundamental physiologic and pathologic principles

As might be anticipated, various modifications of the operation performed by Howard A Kelly in 1893 have been proposed and recommended

Lower in 1914 pioneered the retroperitoneal technique of nephro-ureterectomy as the operation of choice for papillary tumors of the renal pelvis

Judd in 1919 suggested that nephro-ureterectomy should be the routine treatment for papillary tumors of the pelvis of the kidney If the physical condition of the patient does not merit a procedure of this magnitude, a ureteral catheter containing radon seeds may be passed up the ureter following nephrectomy, as recommended by Hess

Statistics vary concerning the percentage of cases in which co existing tumors may be present in the kidney pelvis, the ureter and bladder, varying from 28 to 50 per cent

Dr McDonald first used his technique of nephro-ureterectomy in a patient in whom the ureteral stump, although appearing grossly normal at the time of nephrectomy, subsequently was the site of neoplastic disease

That the retained stump of the ureter may give rise to complications at varying intervals of time following nephrectomy for lesions aside from papillary tumors is evident from reports in the literature

Stepita and Newman have recently reviewed a series of 15 cases of empyema involving the residual ureter

While most ureteral stumps remain quiescent following nephrectomy, and atrophy usually ensues, certain co-existing lesions predispose to chronic suppuration and empyema of the remaining ureter 1) a stricture of the lower end of the ureteral stump with complete or practically complete obstruction, 2) a calculus in the lower ureter, and 3) tuberculous stricture of the lower ureter with a dilated ureter above the point of constriction

In instances in which there is no perceptible obstruction of the lower ureter, muscular atrophy ensues and complications are unusual

In the presence of obstruction, hypertrophy of the muscularis layer occurs, active peristalsis continues, collapse of the ureter is not significant and ureteritis and peri-ureteritis become evident

Such factors must be considered in recommending nephro-ureterectomy I have utilized the technique of nephro-ureterectomy familiar to all of you It permits performing the entire procedure under direct vision, eliminating complications which may occur when what we may call a blind operative technique is employed

I would like to ask Dr McDonald a few questions 1) Can the ureteral orifice be sufficiently occluded by electrocoagulation to preclude the possibility of reopening as the ureter is being freed by blunt dissection? If not, obviously tumor

At times the mobility of the upper flap will seem restricted even though one feels that the technique has been carried out as described. If this lack of freedom is noted posteriorly, it is usually due to an anatomical variation in which the upper portion of the costovertebral ligament sends fibrous slips into the last intercostal muscle fixing it to the spine. This muscle with its nerve and vessels can usually be divided close to the spine avoiding the pleura. If the restricted freedom of the flap is noted in the loin or anteriorly, as is more often the case, adequate extension of the incision across the abdomen in the manner already described is the answer to the problem.

Should pleural injury occur, the tear is usually small and of no serious moment. Simply place a lap pad over the area, notify the anesthetists, and continue with the operative procedure. As a rule it is not possible to suture the fragile pleura as a structure by itself without causing more tears with the suture, or if it is possible to close it, at the close of the operation it may be found that the suture line has reopened owing to the subsequent necessary manipulation. Hence, at the close of the operation, when the wound edges are being brought together, a secure pleural closure is a simple matter by including adjacent fascial or muscle tissue in the pleural stitch. The closure is performed linearly or as a purse-string with a small catheter in the wound. Just before the last stitch is tied, the lung is reexpanded by the anesthetist and the catheter then removed. No particular postoperative treatment or complication is to be anticipated.

The postoperative course in the remaining 42 cases of this series has been entirely uncomplicated. Undue chest pain, respiratory difficulty, prolongation of morbidity, clinical or radiographic evidence of bony deformity were not noted. Early ambulation was encouraged.

The time consumed in developing the flap is not greatly increased, once familiarity is achieved with the technique. The steps follow in ready surgical sequence without going through an elaborate anatomical dissection. Our residents can perform the dorsal component of the incision in 15 or 20 minutes in the average case.

SUMMARY AND CONCLUSIONS

Our experience with the dorsolumbar flap incision has provided adequate exposure in a wide variety of difficult urological cases. This exposure provides the maximum of operative ease to the urological surgeon with consequent maximum surgical safety to the patient.

Acknowledgments Dr. Irving Shiner collaborated in the early operations described in the original series. We wish to thank Dr. Archie Dean, senior consultant in Urology, Veterans Administration Hospital, Bronx, New York, and Dr. Thomas Kirwan, director of Urology, New York Medical College, for their constant encouragement and suggestions. The Medical Illustrations Division, at the above named Veterans Hospital is responsible for the fine illustrations.

ABERRANT RENAL ARTERIES WHICH IN THEMSELVES PRODUCE PAIN

NELSE F OCKERBLAD

There is an extensive literature relating to hydronephrosis produced by aberrant renal arteries. Particularly is this true of those anomalous vessels that enter the lower pole of the kidney below the hilus. It has been stated categorically that one in five persons has extra renal arteries, that is, more than the one usual renal artery. As long as these additional arteries enter the superior pole of the kidney they apparently do no harm.

The case which first called my attention to the possibility of pain arising in the aberrant vessels themselves was one which came under my care a number of years ago. Here was a patient in whom there was a congenital malrotation of the right kidney as shown in the pyelograms (fig 1, A). There was no accompanying

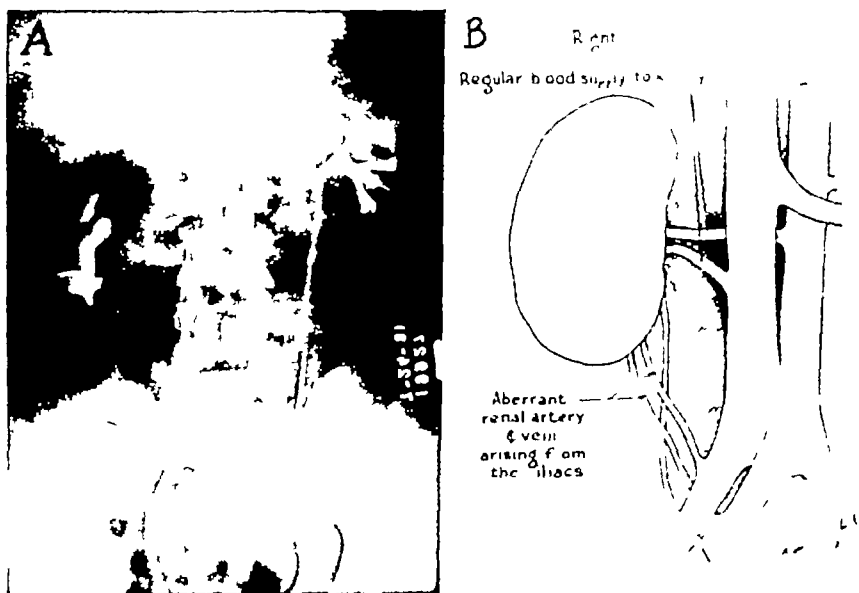


FIG 1 Case 1-1, normal left kidney and right kidney slightly below normal position and with faulty rotation. No evidence of hydronephrosis. B from sketch made at operation. Aberrant renal vessels spring from right common iliac and enter lower pole of kidney. Severing these vessels cured patient.

ing hydronephrosis. At operation, when the area was carefully exposed by dissection, an anomalous blood supply to the right kidney was found. The arrangement of the anomalous vessels was most interesting because in addition to a normal vascular pedicle, an artery and a vein passed from the right common iliac to the lower rounded end of the right kidney. These vessels were stretched taut, and one could see the pulsations of the great vessel being transmitted through these tightly stretched vessels to the kidney. It was apparent that the faulty

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thoraco-abdominal route in the last 3 years. Of these cases, 55 per cent showed at operation local extension of some sort—into the perinephric fat, or into the renal vein, or to nodes about the vascular pedicle or even direct extension through the perinephric fat to the liver.

I believe that I feel more strongly than do Dr. Foley and his associates that the renal vascular pedicle should be ligated just as early as possible, so that there will be a minimum of manipulation of the kidney before the pedicle has been secured. As we all know, in renal tumors of the hypernephroma type there are apt to be tumor thrombi in the large and small renal veins which tend to float into the inferior vena cava and then to produce distant metastases. There is no doubt in my mind that there have been many cases in which such tumor emboli have been literally squeezed from the kidney into the general circulation by the manipulations incidental to freeing up a large renal tumor, especially if the surgical exposure conferred by the wound was somewhat cramped. Therefore I would advocate securing the renal vascular pedicle just as soon as the peritoneum has been dissected from the anteromedial surface of the renal fascia, and before further separation of the kidney. An additional advantage of the early ligation of the pedicle is that this prevents the frequently profuse bleeding which occurs when one of the large veins which may run over the surface of these tumors is torn.

So far, I have been in complete accord with Dr. Foley, but now I am forced to differ with him. In his paper he states: "There have been some bizarre suggestions, such as opening the vena cava to extract from it neoplastic extensions into its lumen—which must be to no purpose." I must admit that tumor thrombus in the vena cava in any given case suggests that thrombi are trying to escape, and perhaps have already escaped. However, I don't see why it goes counter to good cancer surgery to open the vena cava and remove a free-floating tumor thrombus from its lumen. In a case in which this was done 2½ years ago, the patient is still well and apparently free of disease.

In my experience it is unusual for a right hypernephroma to actually invade the wall of the vena cava from the outside. The renal fascia may be lightly adherent to the wall, just as it is to the peritoneum as described by Dr. Foley, but this can easily be separated with patient and gentle dissection. Sometimes, metastatic nodes are adherent to the vena cava, but again these can usually be separated if care be used. Nevertheless there are a few cases where the wall of the vena cava is invaded and where it is necessary to resect the cava. This may or may not be a benign procedure. Although the left renal vein is slightly higher than the right one, they are so nearly at the same level that it may be quite difficult technically to resect the right renal vein and the cava below it without compromising the left renal vein.

I have had the opportunity of making observations on three cases in the last year or so where the vena cava was ligated. In the first case it was ligated as an emergency measure for hemorrhage from a large tear made during nephrectomy for hypernephroma. Although the left renal vein was never visualized, the operator hoped that the ligation was below this. During the 2 days this patient

CASE REPORTS

Case 1 H J W, a 28 year old white man, was admitted to the hospital for study. His chief complaint was pain in his right side. He stated that he could not remember a time when this pain was absent. The pain was, however, relieved somewhat by lying down. He was seldom troubled by the pain at night and had found that he could get comfortable by flexing his right thigh upon his abdomen. Cystoscopic studies showed pus in the bladder urine but none from either kidney. The basis of the pus in the urine was determined to be seminal vesiculitis and prostatitis and that it had nothing to do with the pain in his right flank. The x-ray studies of the kidneys are most interesting.

The pyelograms (fig 1, A) show a normal left kidney and a right kidney slightly below normal position and with faulty rotation. There was no evidence of hydronephrosis. The possibility of a tumor could not be entirely excluded. The condition revealed in figure 1, B was shown at operation. In addition to faulty rotation and adhesions there were two vessels, a vein and an artery from the lower pole of the kidney to the right common iliac artery and vein. These vessels were on a tension and were 8 or 9 cm. long. One could observe the pulsations of the great vessels being transmitted to the kidney through the two anomalous vessels. The vessels were clamped, ligated and severed, the kidney freed and placed in a more normal position. The relief from pain was immediate and permanent. He is still alive and has never had any recurrence of the pain. He survived 4 years of World War II. He has been observed for a period of nearly 20 years without any further trouble.

Case 2 P D R, a 22 year old grocery boy, gave as his chief complaint pain in his left side. He stated that for the past 3 years the pain was practically constant. He stated that from his earliest memory he had suffered from intermittent pain in his left side. During the past several months he had been worked over and a diagnosis of probable renal calculus was made. However, no calculi were ever found. Cystoscopic studies revealed no apparent pathological change in either kidney. From the symptoms alone a diagnosis of aberrant renal artery was made. The left kidney was cut down upon and an aberrant renal artery was found. This artery was clamped, severed and ligated. No other change was found. This patient made an uneventful recovery and has been completely free from pain ever since. Unfortunately the original x-ray film with the pyelograms was lost. He was followed up for a period of 5 years.

Case 3 R H, a 20 year old college student, complained chiefly of pain in his right side. For a month previous to being examined he had an annoying frequency of urination as well as burning on urination. Urological examination showed that the pus in the urine was from the bladder tract. There was a spasm of the ureter on the right so that the ureteral catheter would not pass completely to the kidney. He stated that the past few months the pain in his right side had been steadily increasing. He further stated that he had suffered from pains in his right side off and on for as long as he could remember.

In June 1914, the patient suffered from a cough which was found to be due to a

will solve the cancer problem and make all these radical operations obsolete. Perhaps I should agreeably terminate my remarks here.

But I must call attention to two possibly controversial points.

First, renal carcinomas metastasize, not only through the lymphatics, but also, and even more commonly, through the veins. Therefore we must at the start not only reach and divide the lymphatic drainage course beyond the primary lymph nodes but we must also reach and divide the draining blood vessels before we disturb the renal mass. Dr. Nagamatsu's present description and movie do not clearly show how he reaches the vascular pedicle after raising his flap. Does he approach it from the back, or from the front as so beautifully described by Dr. Foley? Dr. Foley's description is excellent, but I think he should delete the sentence in which he suggests that 'ligation may be postponed until the fascial envelope and its contents have been completely mobilized by separating the posterior leaf of the renal fascia from the muscles of the posterior abdominal wall, diaphragm and vertebral bodies.' Ligation of the pedicle certainly should precede that stage of the dissection. I feel further, that, even before ligation of the vessels, the renal vein and the vena cava should be clearly seen to rule out the presence of tumor inside the vessels. If such tumor extension is suspected one should open the vein and even the vena cava and remove the tumor before clamping. It is much more likely that tumor will reach the vena cava by extension through the renal vein than that it will invade the vena cava by extension through the fat from the lower pole of the kidney.

We all know that in even fairly small 'hypernephromas' the removed specimen may show grossly demonstrable extension of tumor into the lumina of veins. In one instance when I found that the tumor extended through the main right renal vein into the vena cava, I was able through my previously described operation to place rubber-covered clamps on the vena cava just below the diaphragm and below the left renal vein and also on the left renal vein while I opened the vena cava and the right renal vein, removed the tumor, and then sutured the vena cava and ligated the renal vessels. This was all done before disturbing the kidney or its surrounding fat.

My second point is perhaps more controversial. According to most authorities, the diagnosis of malignancy is not always certain. Pyelography, blood sedimentation rate, even arteriography may sometimes leave some doubt. Dr. Prather's paper in the *Journal of Urology* (August 1950) concludes with the statement that 'until a blood or biological test for malignancy is available, surgical exploration is indicated whenever a space-displacing lesion is suspected in the kidney.' The demonstration of malignancy must be made without disturbing, manipulating or squeezing the kidney, but it seems to me that one need not fear opening the renal fascia enough to see dilated veins or other direct evidence or even the surface of the tumor, that is surely safer and more certain than needing for evidence. One would explore and perhaps take a biopsy before undertaking a radical breast operation or a radical operation for cancer of the stomach, or bowel, or even bladder. Perhaps Dr. Foley would agree to this step when in doubt, and perhaps in some doubtful cases Dr. Nagamatsu would

being within a month telling me of her continued good health and freedom from pain for these now nearly 4 years

COMMENT

My thesis here is that in a certain small number of cases, aberrant renal arteries in themselves produce pain. I am well aware that it might be difficult to distinguish between the pain of a kidney stretched by hydronephrosis resulting from obstruction due to the aberrant renal artery and pain arising in the artery itself. Small degrees of hydronephrosis do not ordinarily produce pain. It is probable that the stretching of the renal capsule produces the pain from larger degrees of hydronephrosis. It is well known that a very large hydronephrosis may exist without pain. This is due to the fact that stretching the capsule beyond a certain point or degree causes enough destruction so that there is no pain sensation. The enthusiasts for aortography will at once raise the question of why aortograms were not done in these cases. The answer is simply that I believed a diagnosis could be made without resort to this very interesting but not completely satisfactory diagnostic procedure. I have presented 5 cases which have been gleaned from a large number of cases of hydronephrosis due to aberrant renal artery. There is small doubt that this is a somewhat rare entity. In all these cases here presented, sketches were made of the anomalous blood vessels as seen at operation. In all but one case the x-ray films were preserved. The policy on the part of the x-ray departments of destroying these valuable records is one that often plagues the ambitious urologist.

SUMMARY

Five cases of apparent painful aberrant renal artery are reviewed.

Tension on such anomalous arteries to the lower pole is given as the cause of pain.

The tension may be either of the guy wire type as in case 1 or the supportive type as in case 5.

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possible to treat all those patients. Therefore I am looking forward very much to hearing of your late results in these radical operations, because if these results are significantly better, we shall have to do something about it.

Finally, I would like to thank you all for the very kind and hospitable reception you gave us here, and for the way you entertained us. We had a grand time and learned much from you.

DR B S VALLETT (Wilmington, Del.) I shall confine my discussion to Dr Nagamatsu's paper, and show a few slides of cases wherein we have used his technique.

Dr Nagamatsu has developed a method of unusual merit in the surgical approach to the kidney and adrenal, and is to be commended for his fine work.

(Slide) This was taken to show how the pleura comes down just the same with the rudimentary rib as it does where you have the normal twelfth rib. The dark area here shows the segments of ribs that are often resected and are resected in this technique. We have been in the habit of having the anesthetist hyperinflate the lung when we are working in this region, so we try to keep the pleura in view while we are working.

(Slide) This is a slide of a young woman who had two previous operations, one for renal calculus and one for ureterolysis. This kidney became very badly infected, so we elected to do the Nagamatsu approach here. We did not have to go back through the old incision, and it proved to be a very valuable method in removing this badly infected kidney.

(Slide) This is a slide of a middle-aged woman who had this high-lying left kidney with tumor, and in this case we were able to ligate the pedicle as advocated by Dr Chuté and others, before mobilizing and removing the kidney.

(Slide) This shows another large tumor which proved to be (as we found after we got in) an inoperable tumor. However, I would like to show just what it looked like.

This was the tumor, and after being exposed, we were able here to go down and ligate a very large renal vein and artery before mobilizing this kidney. We did make some attempt to remove all the fat with this tumor, but it was densely adherent to the peritoneum, and even the spleen was involved in this case.

(Slide) This is the tumor after removal. It weighed about 1200 gm.

DR ARCHIE L DEAN (New York, N Y.) My discussion is based on the fact that we still have freedom to practice medicine in this country. I compliment Dr Nagamatsu and Dr Foley on their splendid presentations.

Dr Nagamatsu and I are associated in the Bronx Veterans Hospital, and I have had an opportunity to observe his work at close range. I would like to discuss the use of his surgical approach to the kidney in two groups of patients in which the therapeutic requirements differ.

The first group consists of the common operations on the kidney, such as plastic procedures on the kidney pelvis, operations for stones, nephropexy, and so forth. I don't think I have done any kidney operation for these reasons in the last two years without using the Nagamatsu approach.

stretching out to a greater length and thereby relieve the tension. On the other hand, those aberrant vessels coming into the kidney from a *higher* level could more logically cause pain, just as might result with the renal pedicle itself in the "dragging" caused by marked nephroptosis. Dr. Quinby felt that an aberrant vessel crossing the ureter without obstructing it could cause hydronephrosis as a result of irritative spasm of the smooth muscle of the ureter or ureteropelvic junction.

The problem of sacrificing anomalous vessels requires careful consideration. Anomalous veins may be sacrificed with equanimity, but arteries are terminal, without anastomoses, so that a localized area of anemic infarction results from their loss which may seriously jeopardize the integrity of the kidney if infection should occur. Small arteries may be divided with impunity, but if large, one should first compress them to see how much renal tissue becomes blanched before deciding to sacrifice them. Shupe in 1942 reported an interesting exception to this rule in a case in which resection of an artery the size of a slate pencil extending from the aorta to the lower pole of the kidney did not result in the development of an infarct. The lesson to be derived from this is that it is safer to divide an aberrant vessel to the kidney arising from any other source than the renal artery. I do not know if this is invariably true, because I have not made it a practice to trace anomalous vessels to their origins. It would be of interest to explore this problem further.

tainly goes along with that idea, and we try to do that, including Dr Chute's thoraco-abdominal exposure

I have had informal conversations with many men about this Dr Hess, as far back as 1937, advised twelfth rib resection routinely Dr Bakker tells me that 85 per cent of the renal operations in Holland are done routinely with twelfth rib resections

I want to say one thing about Dr Bakker's questioning the advisability of the radical surgical procedures Dr Sweetser has stated that we all hope the day will come when surgery of this type will not need to be done, because, obviously, the etiologic approach to cancer is the solution, but until that day, in any individual case where you think you can help the patient, I think it is up to us to try to help that patient, even though we know it means only palliation

and where the urine output is necessarily small, the kidney is able to excrete this ion effectively and thus prevent the appearance of hyperpotassemia.

In contrast to its ability to handle excesses of potassium in the plasma, whether from the cells or diet, the normal kidney fails to protect body stores of potassium when deficit occurs. Regardless of the state of cellular potassium, the normal kidney excretes an average of $\frac{1}{2}$ gm. per liter of urine formed, even when potassium intake is zero and hydration and electrolyte patterns are normal. This is not a direct response to any change in plasma potassium concentration. A severe deficit in cell potassium may occur long before plasma potassium concentration falls, and yet when hypopotassemia finally appears, this basal potassium excretion continues, and losses may be greatly in excess of $\frac{1}{2}$ gm. per liter. No adequate explanation is offered for this apparent wastage of the potassium ion, and these losses present a serious problem in replacement when large urine volumes are created by excessive parenteral hydration, for each liter of urine carries with it its complement of potassium ion. In the presence of severe dehydration the kidney thus apparently presents a paradoxical function: beyond its basic excretion of potassium at $\frac{1}{2}$ gm. per liter, it further depletes important body stores, while simultaneously it protects the organism against high plasma levels of the ion that may cause cardiac arrest.

From the foregoing discussion, the conclusion might be reached that potassium excretion by any route, following periods of shock and in the presence of renal shutdown, would improve the patient's prognosis. It has been our impression that the oliguric patients with lower nephron nephrosis do show a higher rate of survival than the anuric group, despite similar courses with respect to replacement control and nitrogen retention. It has also been noted that hyperpotassemia is less common in the oliguric group. Could potassium excretion, in what would seem to be an otherwise useless urine output, be the point of difference?

Figure 1, A depicts the course of a 53 year old woman who was precipitated into renal failure of the lower nephron type by an 18 hour period of intermittent shock, the result of hemorrhage from a ruptured spleen. It might be mentioned, parenthetically, that the urologist interested in renal excretion during the lower nephron syndrome must find patients for study in allied surgical fields, for his own cases commonly follow transurethral prostatic resection and the high concentration of blood in the urine makes any reliable studies impossible. In this patient, the possibility of renal failure occurring following shock was recognized and the diagnosis was made within 48 hours. Characteristically, a phenolsulfonphthalein test at this time came to a "trace" in each half-hour specimen.

Of particular interest is the concentration of potassium in the urine specimen taken 72 hours after the onset of shock. The patient had been of necessity on a potassium-free intake during this time, yet the potassium concentration was elevated to 3 gm. per liter. As has been mentioned, under normal conditions such a potassium-free regimen would have resulted in a basal excretion of around $\frac{1}{2}$ gm. per liter of urine. The kidney was therefore making no serious attempt to conserve intracellular stores of potassium and may well have been attempting to excrete the excess of potassium present in the extracellular space. This



FIG 1 Hydronephrosis and hydro ureter with stricture at lower end of ureter

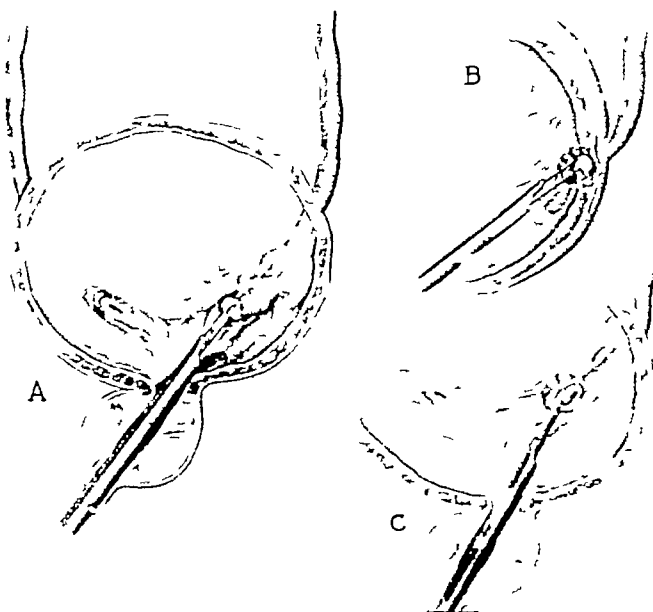


FIG 2 Disconnecting ureter from bladder 1, resectoscope in place in bladder B, resection of ureteral orifice C, sealing ureteral orifice with punctate electrode

the seven days on which urine potassium measurements were made. Had these 2 gm remained in her extracellular space, as would be the case with anuria, her plasma concentrations of potassium would have doubled so that levels of 8 to 10 m eq /liter would have been expected, and the chances of cardiac arrest and death would have been great.

It would seem, therefore, that the lack of potassium conservation by the kidney during oliguria serves a useful purpose. However, during diuresis this usefulness is past. Somewhere between the eleventh and sixteenth days, plasma potassium concentrations fell, and by the eighteenth day the patient showed clinical signs of hypopotassemia. A flame-photometer reading confirmed this impression, showing hypopotassemia to be severe. It is to be especially noted that during this phase, renal excretion of potassium continued to range around 1 gm per liter, despite great deficits not only within the cells, but now in the extracellular space and plasma as well. The potassium losses were accentuated by the large urine volumes, themselves a response to over-enthusiastic fluid therapy in an attempt to wash out nitrogenous end products of metabolism as rapidly as possible. By the seventeenth day, the patient had excreted some 20 gm of potassium without replacement. At this time, diarrhea supervened, with its usual potassium concentration of at least 1 gm per liter, and the acute symptoms appeared. Control of the diarrhea and intensive intravenous potassium therapy at this time produced a spectacular recovery to the point that the patient was able to eat effectively for the first time in 20 days. The rise in plasma potassium concentration from 2.5 to the normal range of 4 m eq /liter tells the story.

Thus, during diuresis the continued losses of potassium in the urine served no useful purpose. Over-enthusiastic administration of fluid in this period with its accentuated urine volume may subtly produce serious consequences. Some of the unexplained deaths that have occurred during diuresis and when the patient was thought to be well on the way to recovery may have been the result of hypopotassemia. It is our practice to give potassium parenterally during this phase if we are not able to stimulate the patient's appetite along the lines of fruit juices, broths, etc. Hypopotassemia is not to be feared in the patient taking a normal diet during diuresis.

SODIUM AND CHLORIDE

In contrast to its handling of potassium, the normal kidney exerts a fine control over sodium and chloride excretion. Excesses are excreted, yet urine salt concentration approaches zero when deficit occurs. However, this ability to conserve salt in the presence of deficit is lost as renal insufficiency progresses especially when the latter is a result of obstructive inflammatory changes in the renal tubules. Our studies on these patients have shown that they may be expected to waste 1½ to 2 gm of salt per liter of urine formed, and this takes place even in the presence of serious salt deficit. Such a wastage of salt becomes of great importance when fluid therapy is aimed at creating large urine volumes in order to reduce plasma nitrogen levels.

The oliguric patient with clinical lower nephron nephrosis has much in com-

Carthv resectoscope with a short beaked sheath, the ureter is completely disconnected from the bladder transurethrally. The first cuts with the loop are made directly over and through the ureteral orifice. Full depth cuts are not made since the thickness of the bladder varies at times. Repeated cuts are made until the bladder wall is entirely cut through and the end of the ureter is seen free in the resected area. During the entire procedure care is taken not to over-distend the bladder. By so maintaining a low intracystic pressure, extravasation of irrigating fluid through the resected hole in the bladder is held to a minimum (fig 2). After the ureter has been fully disconnected from the bladder, a punctate electrode is inserted through a McCarthy panendoscope into the open end of the ureter to seal it off by fulguration. This serves to prevent escape of infected material or tumor cells during the removal of the kidney and ureter. Insertion of a balloon type retention catheter into the bladder is the final step in the transurethral part of the operation.

The second part of the operation is removal of the kidney in the usual manner with the exception that in dividing the renal pedicle the ureter is left attached to the kidney. Then by gentle traction on the ureter and separating it from its bed using long forceps the entire ureter is pulled up through the kidney incision. This is usually accomplished with surprising ease. Care, of course, must be used while separating the ureter from its sheath as it crosses over the common iliac vessels. Once these are clear there is little difficulty. No unusual or troublesome bleeding has been seen as might be expected from blood vessels entering the ureter in its lower third. A Penrose drain is placed in the lower part of the ureteral bed and brought out through a stab wound in the lower abdomen. The kidney wound is then closed in the usual manner (figs 3, 4).

Advantages of this combined transurethral and open operation for complete nephro-ureterectomy are

- 1) The entire ureter, including the orifice and bladder wall immediately adjacent, is removed. This is important in certain renal tumors especially those of papillary origin.

- 2) The operative time is shortened since two incisions are not required. The kidney incision is no different from the usual lumbar incision.

The possible objections that the bladder might not heal or that troublesome hemorrhage might come from small vessels torn from the lower part of the ureter have not materialized. The retention catheter is left in the bladder 14 days. The Penrose drain through a stab wound is left in for 10 days or more. No troublesome bleeding has been observed. It is admitted that only a small number of cases have been done and a better evaluation of this technique can be made after more experience.

SUMMARY

A new technique for nephro-ureterectomy has been presented. By transurethral resection, the lower end of the ureter is disconnected completely from the bladder and the end of the ureter sealed off with a punctate electrode. The kidney and entire ureter are then removed through an ordinary kidney incision.

57 Forsyth St. N W, Atlanta, Ga

nephrosis, a salt excretion of from 2-5 gm per liter takes place, even in the absence of salt intake and in the presence of lowered plasma sodium levels. By definition, urine volumes are those of oliguria so that total salt wastage by this route is not great.

With the onset of diuresis, salt wastage may continue at an average concentration of 2 gm per liter. If urinary chloride measurements cannot be easily followed, it is suggested that a basal salt replacement of 2-3 gm per liter of urine formed be carried out. "Salt losses" of higher concentration than 2 grams per liter were not encountered in this series.

cells or infected urine may be disseminated throughout the pelvis 2) Occasionally the ureteral vessels may be quite large Has he encountered significant bleeding freeing the ureter by blunt dissection not under visual control? 3) At times, due to the presence of ureteritis and peri-ureteritis, the ureter is quite adherent to the iliac vessels Is it a sound surgical procedure to free the ureter at this site not under vision, and has he encountered any complications in separating them by blunt dissection? 4) Is there a possibility of tearing the uterine vessels? 5) Does he believe there is a possibility of establishing a urinary fistula when a fairly large hole in the bladder is not closed and a drain is placed in close proximity to this site?

DR HAROLD P McDONALD It should be emphasized that the success of this operation depends upon complete—and that means complete—disconnection of the ureter from the bladder with the resectoscope at the first stage Unless this is done the second part of the operation will be difficult The rest of the procedure is surprisingly easy

To those who have used the resectoscope in the removal of bladder tumors, and for freeing stones from the intramural portion of the ureter, the disconnection of the ureter from the bladder by means of the resectoscope is relatively easy

In answer to Dr Higgins' questions, there is no doubt but that in many cases fulguration of the ureteral orifice will not occlude it, but in our experience (as will be shown in the movie tomorrow morning) the ureteral orifice was occluded by fulguration Unusual bleeding has not been encountered, in fact no bleeding of consequence has been seen in our small series of cases It would not seem that any should be encountered which would not be controlled easily by packing before insertion of the stab wound drain

It was pointed out that careful dissection of the ureter, as it crosses the iliac vessels, is important As a rule, adhesions are not present to any extent but if present they might cause some difficulty, even from a lower ureteral incision

Urinary fistula has not been seen and should not occur if the retention catheter is left in the bladder for 14 days or so, because the bladder should heal if kept empty for this time If slow healing does occur, it would indicate need for further rest of the bladder by indwelling catheter

anlagen and arise from fetal nests of cloacal tissue. The cloaca of fetal life eventually separates and differentiates into the urinary passage anteriorly and the bowel posteriorly two ways, into intestinal epithelium, or into transitional epithelium. Friedman and Ash concluded "The patches of intestinal epithelium which are not infrequently encountered in the bladder may be derivatives of embryonic cloacal rests. Similarly, the presence of intestinal mucosa and well developed Brunner's glands in the renal pelvis can only be explained by assuming that a rest of tissue with the capacity to form enteric structures was displaced from the cloaca to the ureteral bud."

CLINICAL FINDINGS

Comparatively little is known of the clinical course of these lesions, which are characterized by their asymptomatic behavior. When symptoms occur, there are no recognizable manifestations which differentiate them from other renal tumors. Urinary symptoms are not a constant factor. A large renal mass due to a retroperitoneal hematoma or hematuria may be the only symptom. Surgical exploration, subsequent to urologic studies, is the recommended procedure.

Bell (1946) states that in one-half of the cases of tuberous sclerosis multiple benign tumors are present in the kidney. The co-existence of the tuberous sclerosis complex was present in the case reported by Moolten, one of the cases presented by Inghis, and occurred in 50 per cent of the cases registered with the Armed Forces Institute of Pathology. However, these tumors may be associated with or occur independently of tuberous sclerosis.

Tuberous sclerosis was described by Bourneville and Briassaud (1880) in feeble-minded children with epilepsy and progressive mental deterioration. Since the term tuberous sclerosis refers primarily to the changes in the brain, the broader term tuberous sclerosis complex is therefore employed to denote the co-existence of homologous changes in other organs, notably the heart, kidneys, retina, and skin.

Moolten states "The clinical diagnosis is possible if two or more of the following features can be demonstrated: mental retardation, epilepsy, adenoma sebaceum, phacomia of the retina, multiple mixed tumors (hamartomas) of the kidney, and a familial history of the disease." A very excellent survey of the subject of tuberous sclerosis may be found in the paper by Critchley and Ertl (1932).

I wish to report a case of suspected right renal apoplexy which on exploration proved to be a renal hamartoma. Two of my colleagues, Fuller and Pruett, have recorded me the privilege of including two of their unpublished cases diagnosed at postmortem.

CASE REPORTS

Case 1. M. W., a white woman 23 years of age, who had enjoyed excellent health prior to and during her first pregnancy, was delivered of a normal 9 pound baby, December 20, 1949. It was a rapid delivery, requiring no manual manipulation other than low forceps.

rotation of the kidney was due to these blood vessels arising from the right common iliac I had never before observed a similar renal blood vessel anomaly. These vessels were severed and a few adhesions about the kidney freed and the kidney placed gently back in its bed without any attempt at fixation. The dramatic cure which followed caused me to consider this case carefully and at length I came to the conclusion that probably it was the tension on the artery itself which originated the pain in this case. I then began looking for other cases. Several cases were discovered in the years that followed. One in particular, designated case 5, in this short series (although that would not be its order of sequence)

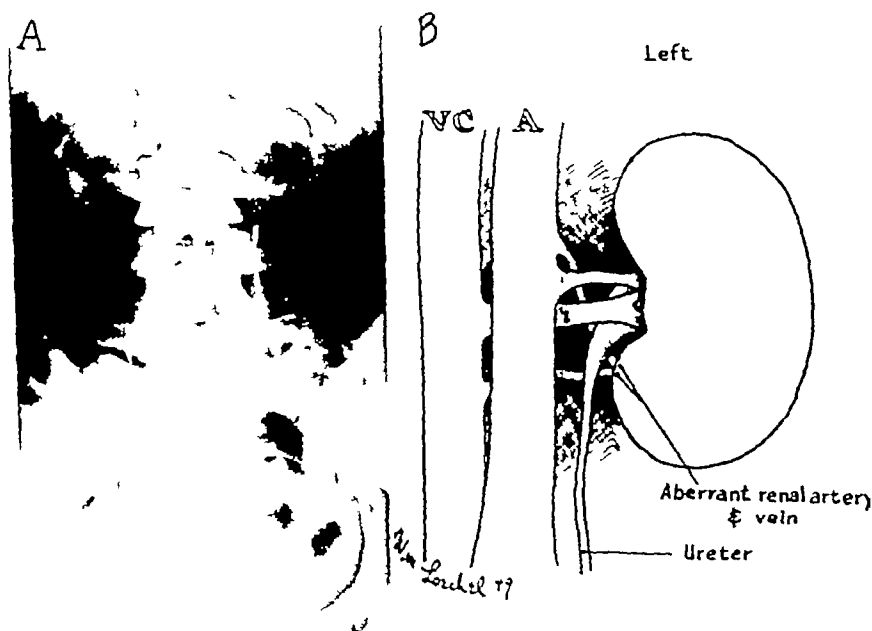


FIG 2 Case 5. A, pyelogram shows slight hydronephrosis. No stricture of ureter. B, another example of what might be termed a weight bearing aberrant renal artery. It arises from aorta well above hilum of kidney and courses downward to point of entrance at lower pole of kidney. Artery undoubtedly was cause of pain.

brought up another point concerning the possibility of arteries in themselves producing pain. Here was found (fig 2) an anomalous renal artery which was supporting a considerable portion of the weight of the kidney when the patient was in the erect position. The artery arose above the kidney and for some perverse reason traversed a course behind the pedicle and was inserted just below the hilum of the kidney in its lower pole.

Thus there were found 2 cases in which it seemed more than probable that tension on an aberrant vessel caused pain, in the one case by having been stretched too tightly while acting as "guy wires," and in the other case having tension by reason of weight bearing. The other 3 cases are some what repulsive but are also corroborative of my thesis.

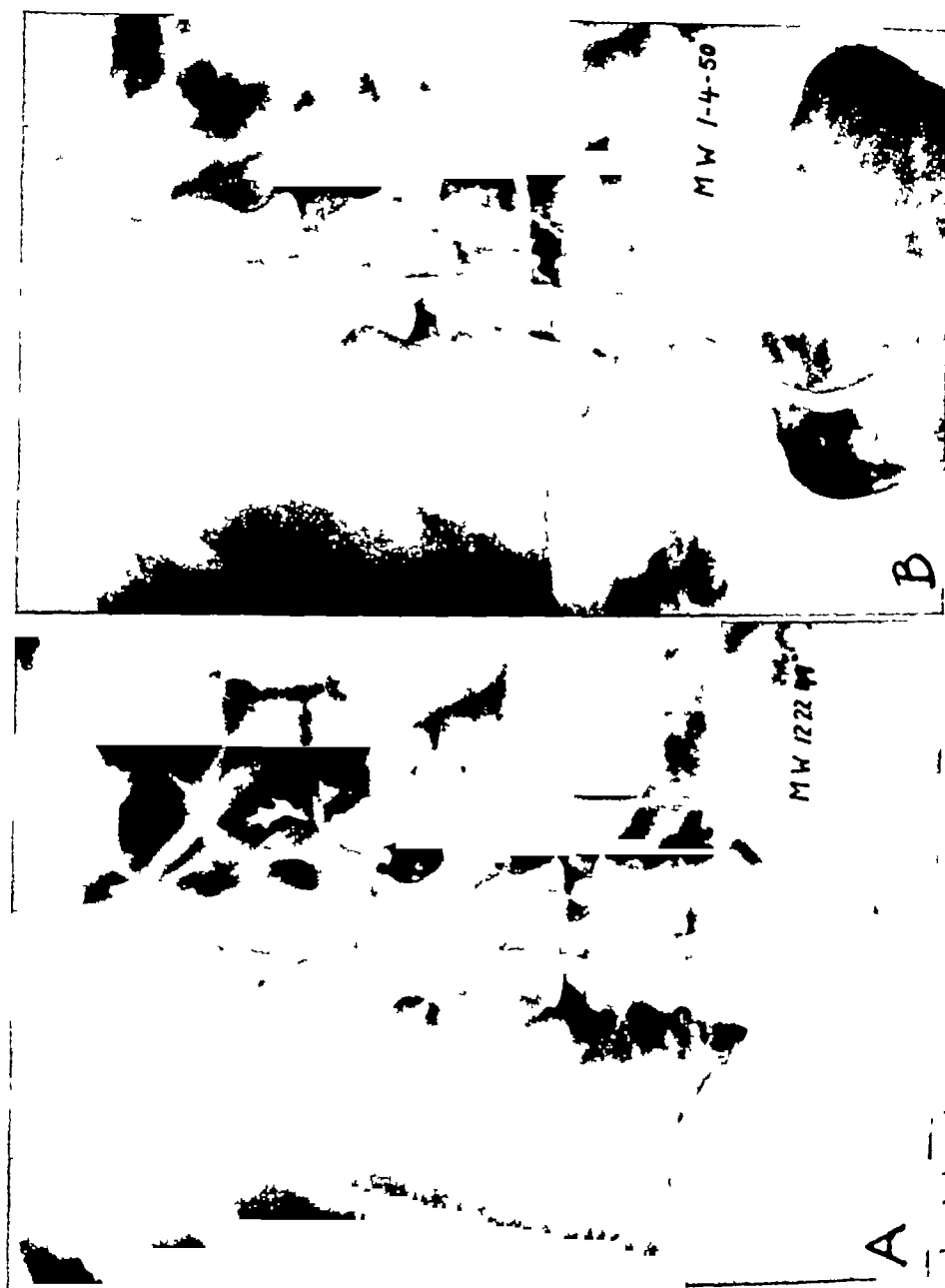


FIG. 1. 1. pycnogram made day following development of right abdominal mass. Obliteration of right pycnogram shadow showing same falling 1 foot. Dictation of middle and lower calyxes and medial displacement of right ureter. 2. right pycnogram 15 days later.

bronchiectases of the left lower lobe. A left lower lobectomy was performed by Dr Clagett at the Mayo Clinic. The possibility of this also being of congenital origin was discussed by correspondence with Dr Clagett.

It was decided to operate upon his right kidney with the diagnosis of aberrant artery to the lower pole. Operation disclosed the artery as suspected. It was clamped, ligated and severed. There was evidence of a small degree of hydronephrosis. This patient made an uneventful recovery and has had no pain since the operation. This patient has gone 3 years without further symptoms.

Case 4 F D, a 34 year old white farmer, complained chiefly of pain in his right side. He stated that for more than 2 years the pain in his right side had been quite constant. Prior to that time he had suffered numerous attacks of pain in his right side. The pain was relieved by lying down. Cystoscopic studies failed to reveal any infection in the urinary tract. X-ray studies showed moderate hydronephrosis in the left kidney, which was not the painful side, and moderate hydronephrosis in the right or painful side. Largely on the basis of symptoms, a diagnosis of painful aberrant renal artery was made. Upon exposure of the kidney it was found that there were three renal arteries. One of these could be identified as the true renal artery. Which of the others was the painful one was the immediate problem. It was decided to sever the most dependent one which had its origin higher on the aorta than the other two. This proved to be the correct selection. The patient has had no more attacks of pain these more than 3 years.

Case 5 L A, a 35 year old single white woman, was sent to me by a urologist in a distant city with the diagnosis of left ureteral stricture. He recommended that she have her ureter dilated. I did dilate the ureter once, and when no stricture was found, I explained to the patient, who was a nurse, that I believed we did not have the correct diagnosis. I recommended a complete review of her case. Her complaint was pain in her left side in front radiating downward and she could not remember a time when she was completely free from the pain. The pain disappeared nearly always upon lying down. There were times when it was necessary for her to sit still for some time and on such occasions she always chose a straight backed chair and would obtain a little relief from pain by putting a thick book between the chair and her back.

It was 4 years before she returned to me, after being out of town, willing then to allow me to do a complete urological examination. From the data obtained in this examination it was determined that there was an aberrant renal artery to the lower pole of the left kidney without appreciable hydronephrosis (fig 2, A). A short time later her left kidney was operated upon by me. Upon exposing the kidney the artery causing the pain was easily seen. It came from a point higher on the aorta than the normal pedicle and coursed diagonally, outward and downward behind the normal renal vessels and the ureter. It was plain to be seen that in the upright position this vessel carried a considerable portion of the weight of the kidney (fig 2, B). The anomalous artery and its accompanying vein were ligated and severed. Nothing was done to improve the position of the kidney. This patient made an uneventful recovery and has had no pain whatever since the operation. She writes the most appreciative letters, her most recent one

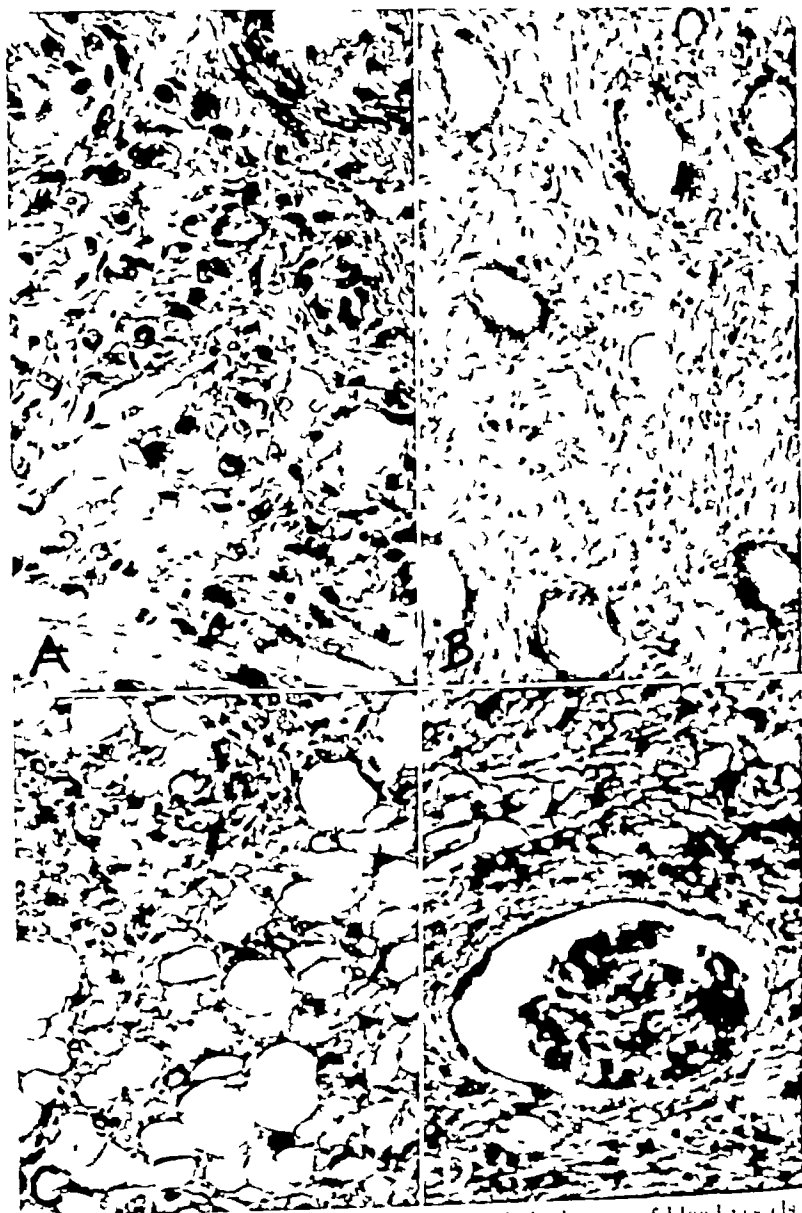


FIG. 4. Case 1. *A*, shows marked proliferation and thickening of blood vessels, muscle fibers and fat cells $\times 150$. *B*, compressed tubules and blood vessels with marked leukocyte infiltration $\times 72$. *C*, number of mature fat cells and strands of muscle fibers $\times 72$. *D*, tumor has compressed renal parenchyma. Infiltration surrounding glomeruli $\times 100$.

the kidney parenchyma is well demarcated but there is no capsule. A few glomeruli and tubules are incorporated within the edge of the neoplastic tissue, although this could not be interpreted as frank infiltration.

The growth obviously falls into the category of the angiomyolipomas and sarcomas which are rare but characteristic hamartial tumors of the kidney (fig 4—1 *B*, *C*, *D*).

DISCUSSION

DR THOMAS E. GIBSON (San Francisco, Calif.) Dr Ockerblad has introduced a new concept in attributing renal pain to aberrant renal vessels which are not obstructive to urinary drainage.

The mechanism of renal pain is a difficult one to evaluate by either clinical or experimental methods. There are two types of renal pain: 1) the intermittent, colicky type due to spasm of the smooth muscle component of the pelvis, calyces and ureter, and 2) the more or less continuous dull ache as seen in acute renal and perirenal infections (such as renal carbuncle and perinephric abscess), and also in some cases of nephroptosis where the pain is presumably due to "drag" on the renal pedicle with or without torsion. I doubt that stretching of the renal capsule, or diseases involving the renal parenchyma primarily, are an important cause of renal pain. If such were the case, why should large renal tumors so often be painless? Pain in renal tumor, when it occurs, is generally due to encroachment on the calyces or to passage of blood clots down the ureter causing obstruction or interference with urinary drainage with consequent smooth muscle spasm. It is noteworthy that the various forms of Bright's disease, in which the renal parenchyma is largely destroyed, are usually painless. The liver is analogous, in that biliary colic is due to affections of the bile ducts and not to conditions affecting the liver parenchyma or capsule.

We often see patients with a pain in the general region of the kidney where we are called upon to do a complete urological investigation to determine whether the pain is renal or extrarenal. Even then, it is sometimes difficult to definitely evaluate the role of the kidney in a given case. It is especially confusing if the study is entirely negative and yet the patient says the pyelogram reproduces the same pain. Pain reproduction is not always a reliable guide. One patient of mine stated that the pyelogram reproduced the pain on her left side when the actual cause was a carcinoma of the left colon.

Nephralgia of unknown origin is the designation given to painful kidneys in which no organic defect can be determined and extrarenal sources of pain have been eliminated. Some years ago in the *Journal of Urology* I published the report of a small series of such cases in which, with some trepidation, renal denervation (sympathectomy) according to the method of Papin was performed. Most of these patients were relieved of their pain even though at operation the cause of the pain was not disclosed. I wonder if in Dr Ockerblad's cases the severing of sensory nerve fibers incidental to mobilization of the kidney may not have relieved his patients' pain, rather than dividing the aberrant vessels. To get at the vessels, as he has done, and to explore their origins, would call for a pretty thorough nephropelvio-ureterolysis. It is difficult for me to envisage relief of pain by cutting an aberrant vessel entering the kidney from a lower level, since the kidney with its natural mobility tends to gravitate downward, a fact which would tend to counteract any guy wire traction on the vessels. Furthermore, one would think that such vessels would themselves compensate by

revealed the presence of multiple, sharply circumscribed and somewhat globular, soft, friable, opaque, yellow-brown tinted nodules which varied from 0.7 cm to 1.5 cm in diameter. These nodules, although sharply circumscribed, were not encapsulated. Approximately one dozen of these peculiar nodules were haphazardly distributed in the substance of the kidney. There was no deformity of the renal pelvis.

Microsections of the nodules disclosed nonnative tissue resembling adipose tissue of the adult type. The nuclei were abnormally conspicuous and hyperchromatic and showed more than normal variation in size and shape. The cytoplasm of these cells was occasionally not completely washed away, and certain cells were quite distinctly spindle-shaped and were arranged parallel with a vague tendency towards bundling. The vessels are thick-walled. In many places the vessels lie in the fat where they are surrounded by collars of immature muscle fibers (fig 5—A, B).



FIG 6 Case 3 Hamartoma with compression of parenchyma. Showing fat cells, muscle fibers, and compressed glomeruli. $\times 72$

Case 3—L. B., a woman 76 years of age, was admitted to the hospital March 13, 1949, and died 3 days later. Eight hours prior to admission she developed severe abdominal pain, associated with nausea and vomiting. As in the preceding case there were no genito-urinary symptoms. Physical examination revealed an acutely ill woman, in myocardial failure with generalized edema and ascites.

The postmortem diagnoses: acute bronchitis, lobular pneumonia, intestinal obstruction, atherosclerosis, cholecystolithiasis, *large (angiomylipoma) hamartoma of the left kidney*.

Embedded in the substance of the lower pole of the left kidney was a sharply circumscribed but nonencapsulated globular tumor mass which measured slightly less than 1 cm in greatest diameter. The opaque, yellow-gray tinted substance of this tumor is extremely friable. The microscopic sections showed a renal hamartoma, and the diagnosis was confirmed by the Tumor Registry of the California Society of Pathologists, and California Cancer Commission. The tumor revealed a mixture of several kinds of unripe tissue of mesenchymal origin. There

SODIUM AND POTASSIUM EXCRETION WITH NEPHRON NEPHROSIS

RICHARDS P. LYON AND DONALD R. SMITH

*From the Division of Urology, University of California School of Medicine,
San Francisco, Calif*

Lower nephron nephrosis has become a familiar entity to the urologist, because the differential diagnosis of anuria and oliguria, especially following shock, always includes this type of renal failure. Because the lesion is reversible, if allowed 10 days to 2 weeks for repair, specific therapy is directed at maintaining a normal status in terms of fluid, electrolytes, and nutrition. The present study was stimulated by the observation that oliguric patients with "lower nephron nephrosis" seem to have a greater chance for survival than the anuric group. Expecting to find an answer in the urine itself, we carried out a series of observations on 6 patients with varying grades of oliguria. In order to demonstrate the overall trends observed in this study, the course of one of these patients will be described in some detail. This patient was unique in providing not only an excellent study in terms of the course of lower nephron nephrosis, but in supplying data as to renal function during periods of both salt and potassium deficits when renal tubular damage is great. In order that the clinical implications may be appreciated, discussions of the electrolytes potassium and sodium will precede the clinical data.

POTASSIUM

The concentration of the potassium ion is relatively low in the plasma and extracellular compartments, and normally ranges from 4 to 6 m eq /liter. The opposite situation exists within the cell, for here the concentration is 35 times that of the plasma, or 150 m eq /liter. Fifteen liters of fluid make up the average extracellular space with its plasma component, so that the extracellular compartment contains only 3 or 4 gm of potassium in contrast to the 180 gm present within the cells. With such a potassium distribution, if a relatively small amount of potassium were to leave the cells and pass into the surrounding extracellular space and plasma, a precipitous rise in plasma potassium concentration would occur. Thus, if only 3 of the 180 intracellular grams of potassium should move out of the cell, plasma potassium concentration would be doubled. Cardiac arrest and death could result, a situation always to be feared after the seventh day of anuria.

Such a movement of potassium from the cell to the outside, along with cell water and products of cellular catabolism, does occur in association with shock, dehydration, surgical trauma, and other conditions typified by an "alarm reaction." If the patient is to tolerate movement of potassium into the plasma, some mechanism of potassium excretion must come immediately into play. The normal kidney handles the problem efficiently. It rapidly excretes potassium at concentrations in the urine up to 50 times that of the plasma. Even with severe dehydration where the movement of potassium from cells to plasma is excessive,

Read at annual meeting, Western Section American Urological Association, Sun Valley, Idaho June 27, 1951.

THE PROBLEM OF THE NONOPAQUE URINARY TRACT STONE

S RICHARD MUELLNER AND BERNARD STARS

Nonopaque renal or ureteral stone may at times present unusual diagnostic and therapeutic difficulties. The search for the cause of acute pain, hematuria, or chills and fever can be completely misdirected by the inability to identify or localize the stone. A few brief case reports will serve to illustrate this point.

CASE REPORTS

Case 1 G F, aged 54, BIH No M 5820, entered the hospital because of a sudden, sharp, nonradiating pain in the right lower quadrant, associated with nausea and vomiting. Tenderness and muscle spasm were present in the right lower quadrant. The white blood cell count was 23,800. Urinalysis: 2-4 red blood cells per high power field. A diagnosis of acute appendicitis was made, but because of red blood cells in the urine, a plain film of the abdomen was taken. This was negative. Cystoscopy was, therefore, done. A small, brownish calculus was seen just within the right ureteral orifice. Blood uric acid amounted to 5.4 mg per cent and 6.5 mg per cent respectively. This patient narrowly missed an unnecessary appendectomy.

Case 2 S R, aged 66, BIH No M 17339, was admitted for painless hematuria. For the past 2 years, he had repeated attacks of gross painless hematuria. A complete urologic investigation elsewhere failed to disclose the cause of the bleeding. The physical examination was negative. The urine contained 30-40 red blood cells per high power field. Blood uric acid was 7.8 mg per cent. An excretory urogram showed a nonfunctioning right kidney. In the retrograde pyelogram many small rounded filling defects in the calyces, pelvis, and upper ureter were seen (fig. 1). These were considered to be due to either papillary tumor of the pelvis, pyelitis and ureteritis cystica, or nonopaque stones. At exploration the negative shadows proved to be uric acid stones.

Case 3 S W, aged 61, BIH No M 15498, was first admitted March 20, 1950, because of gross hematuria and transient burning and pain at the meatus. The physical examination was negative. Urinalysis: 50-60 red blood cells per high power field. The blood uric acid was 4.4 mg per cent. An excretory urogram was normal. A retrograde pyelogram raised suspicion of a nonopaque ureteral stone. The second admission was October 16. The patient had a temperature of 101°F. For eight days he had pain in the right costovertebral angle, pain, nausea, vomiting, and one episode of gross hematuria on the day before re-entry. An excretory urogram done elsewhere was negative. When it was repeated at the hospital it showed a nonfunctioning right kidney. Retrograde pyelogram disclosed moderate right hydronephrosis and raised the question of a nonopaque stone. Because of the uncertainty another retrograde pyelogram was done a few days later. On this occasion the examiner felt a "grating sensation" against his catheter 2½ inches up in the ureter and believed it to be due to a nonopaque stone. The blood

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potassium concentration then fell to a little over 1 gm per liter and remained between one and two during the remaining 7 days of oliguria. Significantly, plasma potassium levels never rose above 6 m eq /liter

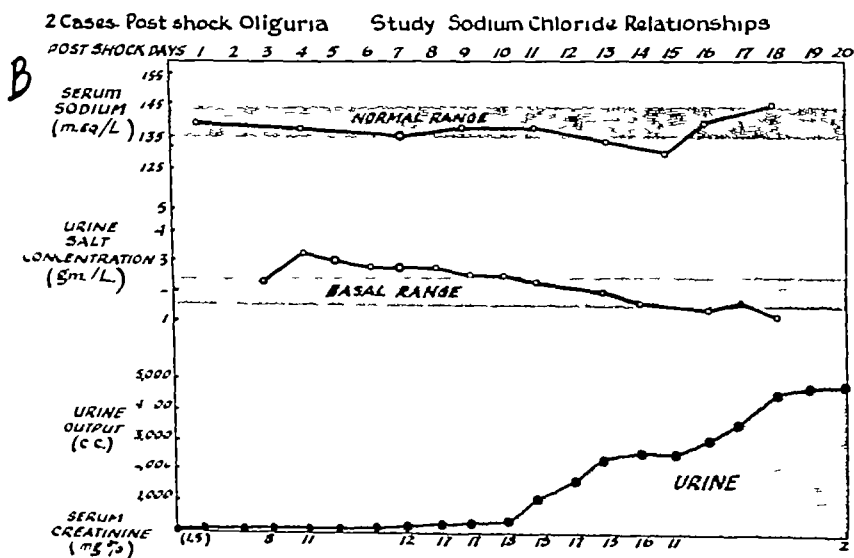
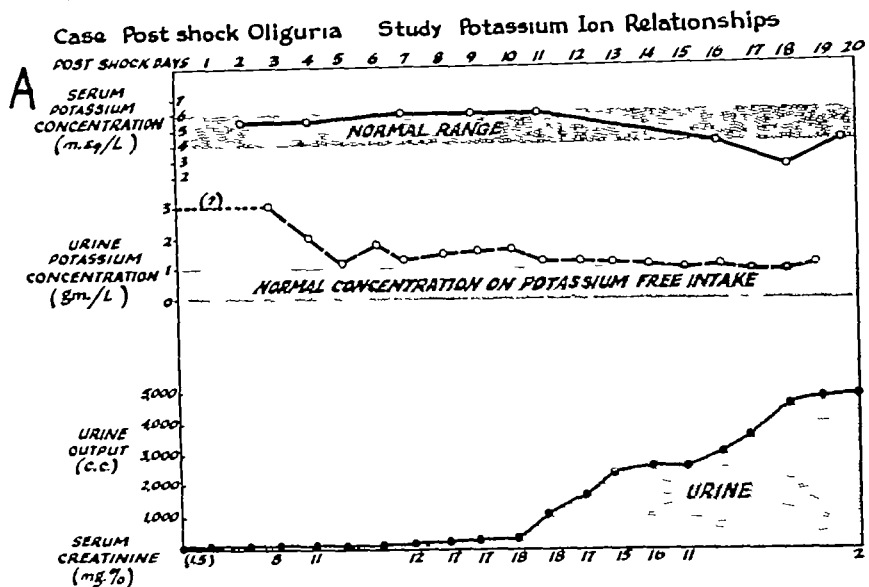


FIG 1

Thus, the apparent ability of the kidney to excrete this ion, when it finds its way into the extracellular space and plasma during the oliguria of lower nephron nephrosis, may be a decisive factor in mortality differences between the anuric and oliguric patient. In this case, at least 2 gm of potassium were excreted during

eterization, to chronic glomerulonephritis, or to polycystic kidneys. The patient was given intravenous fluids. He promptly developed pulmonary edema and bronchopneumonia, and died. Autopsy showed that both ureters were blocked with yellowish, nonopaque stones. Many smaller stones were found on the renal papillae of both kidneys.

DISCUSSION

These case histories taken from a group of 24 cases demonstrate the nature of the problem which an invisible stone presents.

From a clinical point of view this problem could be simplified, if one knew when to suspect a nonopaque stone, and how to identify it. Analysis of our material suggests that a nonopaque stone should be considered in patients who have gross or microscopic hematuria associated with renal or ureteral pain in the presence of a negative plain film of the abdomen (kidneys, ureters and bladder) or excretory urography. Faced with such a case, it may be helpful to check the level of the blood uric acid. A level of 5 mg per cent or higher was found in about one-third of our cases and served as a useful clue suggestive of a nonopaque calculus.^{1,2}

While 11-20 per cent of patients with gout form uric acid stones, it is remarkable to find a fairly high percentage of patients who have no history or clinical evidence of gout and who have, nevertheless, an elevated blood uric acid level.^{3,4}

About 6-8 per cent of urinary tract stones are nonopaque to the x-ray and in that group uric acid stones predominate. For clinical purposes, therefore, the nonopaque stone and the uric acid stone are practically synonymous. It will be helpful to summarize some of the salient facts pertaining to uric acid calculus.

Uric acid stones are commonly single. Only three of our patients had multiple uric acid stones. The stones are apt to be small, probably due to the fact that a comparatively small amount of uric acid is excreted daily in the urine (1 mg in 24 hours). These stones grow slowly by accretion, and the crystals which combine to form them are very small and quite compact.⁵ Uric acid stones are primarily of metabolic origin, in contrast to stones which are secondary to obstruction or infection. The small uric acid stones will, therefore, in most instances pass through a structurally normal urinary tract. We shall return to these facts when we discuss the management of nonopaque stones.

How best to visualize a nonopaque stone is as yet an unsolved problem. There is not a single universally successful method which would demonstrate the size and position of such a stone. All methods in use have been accompanied by success and failure, failure not only to show the stone, but to differentiate it with certainty from noncalcareous matter which also casts a negative shadow.

The excretory or retrograde pyelogram may show a negative filling defect. A

¹ Peters and Van Slyke, *Quantitative Clinical Chemistry*, Baltimore: Williams & Wilkins, 1946, 2nd ed., vol. 1.

² Suby, H. I., *Med. Clinics North Amer.*, **91**, 1315-1332, 1948.

³ Brown, J. and Mallory, G. R., *Eng. J. Med.*, **243**, 326-329, 1950.

⁴ Tilbott, J. H., *J. Clin. Investigation*, **19**, 645-648, 1940.

⁵ Jacobson, B. M., *Ann. Int. Med.*, **11**, 1277-1295, 1948.

⁶ Price, I. L. and Frondel, C. J., *Urol.*, **57**, 919-931, 1947.

mon with these "salt-wasting" patients. Urine salt concentrations for the characteristic patient are shown in figure 1, B. Here, during oliguria, salt concentrations ran from 2 to $3\frac{1}{2}$ gm per liter despite considerable variations in plasma sodium concentrations and a salt free intake. The finding of an ample basic salt excretion of 2 gm per liter has been relatively constant in lower nephron nephrosis, even when plasma sodium levels are less than 130 m eq per liter (normal 140 m eq / liter).

Wastage of sodium chloride during the phase of oliguria at the rate of 2 gm per liter would, in itself, probably create no serious electrolyte imbalance. However, it is our practice to measure the daily losses, when possible, and to replace them. This measurement is simply and accurately made with the chloride test described by Schiles and Schales and modified for bedside use by Scribner. The chloride test as a measurement of total salt content seems to be especially accurate in the patients with severe tubular damage. Perhaps the failure of ammonia formation leads to obligatory excretion of sodium with the chlorine ion.

During diuresis the renal control of salt excretion may change. As is demonstrated in this figure 1, B, salt concentration fell to 1 gm or less per liter soon after diuresis began. The patient was in salt deficit at this time as a result of extrarenal salt losses and inadequate salt replacement. That the kidney can excrete such a low concentration of salt when conservation of body salt is needed is evidence against the generally accepted view that large amounts of salt are necessarily lost at this time. No case in our series has excreted more than 2 gm per liter unless extra salt has been given. It would appear, therefore, that the large salt losses to be feared are those from the gastro-intestinal tract and those excreted in immense urine volumes where salt concentration may be as high as 2 gm per liter.

SUMMARY

Potassium The normal kidney effectively excretes large excesses of the potassium ion, protecting against high plasma potassium levels that could be fatal. However, the normal kidney does not have the ability to conserve potassium when deficit occurs so that an average of $\frac{1}{2}$ gm of potassium is wasted in every liter of urine formed. These losses continue even when plasma concentrations have reached fatally low values.

The present study suggests that during the oliguria and diuresis of lower nephron nephrosis the kidney appears to differ little in function from the normal. Potassium excretion in the small urine volume of the oliguric phase may be sufficient to prevent plasma loss from reaching fatally high levels. However, this usefulness, which is lost during diuresis for potassium wastage in large artificially-created urine volumes (as would occur with the normal kidney as well) may lead to hypokalemia and death. The patient will be benefited by less aggressive attempts at hydration during diuresis and by a potassium intake adequate to replace urine losses.

Salt The normal kidney can excrete large excesses of sodium chloride as well as decrease urine salt concentration to negligible quantities when deficit occurs.

The present study demonstrates that during the oliguria of lower nephron

With the segment of ureter within the reach of the operative wound, normal to palpation, the surgeon now faces the unhappy decision to explore the ureteral lumen through a ureterotomy by means of bougies, to end the operation altogether, or to review the remainder of the ureter through a new incision with perhaps the same results. It would seem wise to undertake surgical exploration on the basis of two indications, blocked urosepsis, and on suspicion of tumor.

The following case taken from the records of the Boston City Hospital illustrates how troublesome lithotomy for a nonopaque stone can be.

A P., aged 41, BCH No. 1376289 was admitted June 22, 1950 because of pain in the left costovertebral angle. The physical examination was negative. The urine was concentrated and contained 18-24 red blood cells per high power field. Cystoscopy on June 23 showed a moderately dilated left renal pelvis and left ureter. There was a filling defect in the lower one-third of the ureter and at the ureteropelvic junction suggestive of nonopaque stones. At operation by the house staff on June 26, the kidney was first explored through a lumbar incision. No stone was found in the pelvis and in the ureter as far as it could be palpated. This wound was then closed and the remainder of the ureter down to the bladder was explored through a Gibson incision. No evidence of stone was found. The ureter was opened and bougies were passed without meeting obstruction. This wound was, therefore, closed and immediately following operation, a cystoscopy was done. This showed a lacerated left ureteral orifice and small pebbled stone in the bladder.

SUMMARY

Nonopaque stones most commonly consist of uric acid.

No infallible method to demonstrate the presence, the size, and the location of a nonopaque stone exists today.

A blood uric acid of 5 mg. per cent or more is suggestive of a uric acid stone in patients who have questionable renal pain, hematuria, and negative x-ray studies of the upper urinary tract.

Uric acid stones usually occur singly in a structurally normal urinary tract and are apt to be small. They seldom lead to severe damage of the urinary tract.

Conservative management is advisable in most instances.

Surgical intervention is indicated when a stone blocks drainage from an infected kidney or when it cannot be differentiated from a tumor of the pelvis or ureter.

We want to thank Dr. Prather for permission to include his private patient and for allowing us to study the case records at the Boston City Hospital.

520 Beacon St., Boston, Mass.

RENAL HAMARTOMA (ANGIOMYOLIPOMA) REPORT OF THREE CASES

CARL RUSCHE

Hamartomas have been reported in most organs of the body, perhaps the most common site being the lung with renal involvement of infrequent occurrence. The earliest recognition of this tumor is credited to Chiarì (1883) who termed it lipo-chondro-adenoma. Albrecht (1904) called this complex structure hamartoma, or "error tumor," and described it as a lesion formed by normal tissue elements which are abnormal only in their quantitative value. The deduction to be drawn from histological examination of these formations is that they have originated in an abnormal mixing of the tissue elements, or from disturbance in their development.

From the available data, scientific textbooks and a review of the world literature, renal hamartomas have been considered a comparatively rare lesion, although the actual index of incidence is believed to be much higher because many of the lesions are never diagnosed. Ordinarily, they are incidental findings at postmortem. Friedman is of the opinion that many of these tumors, which generally are only a few millimeters in diameter, go unnoticed in histopathologic examinations of renal specimens removed surgically and at autopsy. Thorough investigation of minute filling defects revealed in pyelograms might disclose the presence of these neoplasms in some instances.

Von Lichtenberg, Voelcker and Wildbolz (1926-1929) reviewing the world literature, recorded no instance of renal hamartoma. The few cases of recent date which have been reported may be of noteworthy significance. Moolten (1942) reported an occurrence in a 15 year-old girl, Mallory (1949) observed one in a woman 39 years of age, both cases were diagnosed as a result of renal symptoms. One of the cases which Inglis (1950) reported in a 56 year-old woman manifested clinical symptoms, the other case, a 41 year-old woman, was an incidental postmortem finding. In the Registry of the Armed Forces Institute of Pathology there are 52 cases of renal hamartoma, all occurring in males, 44 were found at autopsy, and 8 manifested clinical symptoms.

ETIOLOGY

From the varied histologic formations, the presence of abnormal and normal tissue, it is impossible to determine whether hamartomas should be classified as an anomaly of development, or a true neoplasm. Although these lesions are composed of mixed elements they are not true teratomas, which contain other elements such as hair, squamous epithelium, and nerve cells, none of which are present in hamartomas. The lack of mitotic figures, the noninvasiveness and nondifferentiation, and the apparent absence of metastases in the cases which have been studied, are characteristic of a benign tumor.

Inglis has suggested tissue predisposition from germinal transmission as a causative factor. It is assumed that these tumors have their origin in aberrant

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be uric acid stones, and have proven to be very hard, so that they were extremely difficult to crush readily by transurethral methods

(Slide) Here is an example of a large filling effect in an air cystogram, which proved to be a medium multiple prostate, and here (slide) is an example of a uric acid stone which was crushed. Ordinarily, however, they are best removed by suprapubic means

Dr J SYDNEY RITTER, (New York, N Y) Dr Muellner has given us an excellent discussion of the unusual diagnostic and therapeutic difficulties associated with the management of renal and ureteral uric acid calculi. By means of concrete examples he emphasizes some of these

The differential diagnosis between nonopaque stone and blood clot, tumor, desquamated epithelial cells, air bubbles either originating in the urinary tract or introduced through a ureteral catheter and ureteritis cystica may not be easy. Moreover, difficult types of calculi may be nonopaque—cystine, xanthine, sulfonamides, soft, small, calcium stones. It is only by a complete urologic survey that the correct answer will be obtained. Certainly in doubtful cases with anuria, such as case 4, the question of obstruction should be raised and adequately managed by diversion of the urinary stream if this seems indicated.

Certain points should be emphasized. Although ordinarily uric acid calculi are small, they may be large and associated with severe renal damage. In such cases differential diagnosis between soft phosphatic calculi, cystine calculi and tumor may be extremely difficult.

Dr Muellner has not mentioned in his discussion of the nonopaque urinary stone, some of the problems related to this type of calculus in the bladder. Nonopaque urinary calculi occur in the bladder about as frequently as they do in the upper urinary tract. They ordinarily cannot be seen on the plain film but show up well on the air cystogram. When they show up on the air cystogram they must be differentiated from a discrete median lobe of the prostate, from a bladder tumor and from blood clot. Usually this is not too difficult although, occasionally, a definite differential diagnosis cannot be made from the x-rays alone and cystoscopic examination is necessary. It is my feeling that in practically all cases, before definite treatment is indicated a cystoscopic examination should be done to be sure of the nature of the situation in the bladder. Ordinarily this is the most satisfactory examination to rule in or out the presence of such a stone.

Nonopaque calculi in the bladder are practically all uric acid stones. These stones, in my experience, have been extremely hard and very difficult to crush because of their extreme hardness. For this reason, if the stone is over 2½ cm in diameter on the x-ray films, it might be wise to remove the stone by open surgery. It might be wise to remove the stone through open surgery if adequate armamentarium in the form of all types of lithotrites of adequate strength are not present. It is the type of stone upon which one may occasionally break a lithotrite because of the hardness of the stone. In contrast, phosphatic calculi of much larger size can be readily treated by litholapaxy because of the relative brittleness and softness of the stones.

In conclusion, I wish to emphasize again what Dr Muellner has emphasized that the nonopaque urinary calculus presents unusual diagnostic and therapeutic difficulties. It must be diagnosed from blood clot, tumor, desquamated epithelial

Approximately 12 hours postpartum, the patient was awakened by a dull pain in her right side. She complained of shortness of breath, palpitation, pallor and sweating. The symptoms were in keeping with internal hemorrhage. The physical examination demonstrated a large mass in the upper right quadrant of the abdomen, which did not fluctuate, was moderately firm in consistency, and only slightly tender.

The prothrombin time was 56 per cent of normal, hematocrit test was 22, and clot retraction was normal. The urine was grossly clear but loaded with red blood cells. The white cell count was 15,800, erythrocytes 2,800,000, and the hemoglobin was 9 gm.

Cystoscopic examination the following day revealed a normal bladder. Ureteral catheters were readily passed to each renal pelvis. Indigo carmine injected intravenously appeared in four minutes from each kidney, with marked reduction in dye concentration from the right. Roentgenograms disclosed a soft mass in the right renal area. The right pyelogram showed displacement toward the right upper quadrant of the abdomen with distortion of the lower calyx. Only the upper and middle calyces were visualized. There was medial displacement of ureter and obliteration of psoas shadow (fig 1, A). The left kidney and ureter showed no departure from normal.

The blood studies showed no improvement following two blood transfusions and a course of vitamin K therapy. Clinically, the mass in the right renal area had undergone no change in two weeks. The patient continued to complain of slight abdominal discomfort, and microscopic hematuria.

Retrograde pyelograms made on the fifteenth day postpartum showed the same changes demonstrated 2 weeks previously (fig 1, B). The preoperative diagnosis was renal apoplexy probably associated with renal neoplasm. The possibility of tumor was seriously considered.

On the seventeenth day postpartum, a surgical exploration was carried out. Upon exposure of the kidney, a large, reddish mass, apparently a large hematoma, was encountered. Following the removal of the organized blood clot, the kidney was readily palpated, the lower pole was irregular, firm, and enlarged consistent with neoplasm. Nephrectomy was performed. The gross specimen consisted of the right kidney measuring 17 by 15 by 16 cm with 13 cm of the ureter attached. The lower one-half of the kidney surface was irregular, rough, and presenting numerous large cavities filled with hemorrhagic material (fig 2). On section, a discrete, nonencapsulated, yellowish tumor mass with marked necrosis and hemorrhage occupied the lower half of the kidney. The kidney pelvis was not involved by the tumor mass. The upper pole of the kidney appeared normal (fig 3). The histopathologic diagnosis was renal hamartoma. Microscopic sections were submitted to Friedman, formerly with the Army Institute of Pathology, for confirmation of diagnosis.

Pathologic report (Friedman): "The tumor consists of three intermingled components, fat, blood vessels and bundles of smooth muscle. Much of the fat is adult adipose tissue but there are many clusters of embryonal fat cells particularly about the vessels. The vessels are predominantly thick-walled, small arteries

jagged scratches caused by the stone. It is usually necessary to examine the bulb through a lens. We find it a very valuable diagnostic method.

In this connection, we also find that putting a wax tip on the end of a catheter very often facilitates its passage up the ureter. Sometimes the sharp end of the catheter will catch in the ureter wall and will not pass on up. Just dip it in wax, and often it will pass readily.

DR THOMAS D. MOORE (Memphis, Tenn.) Drs. Muellner and Sears are to be commended for their timely discussion of difficulties encountered in the management of nonopaque urinary stones. It is interesting to hear Dr. Ormond call to your attention the use of the wax bulb in the ureter. This measure is not only of great value from a diagnostic standpoint but occasionally it may prove of value therapeutically as illustrated by the following recent experience. A general surgeon referred his nephew for a urologic examination after having made a tentative diagnosis of acute appendicitis. There were a few red blood cells in the urine, the initial film of the region of the urinary tract was negative.

The surgeon stood by while a cystoscopic examination was made for the purpose of ruling out a ureteral calculus. There was absence of secretion from the right orifice. A ureteral catheter with a wax bulb at its tip met in obstruction 3 or 4 cm. above the orifice when steady pressure was maintained for a few seconds, permitting the bulb to pass the obstructed point. Upon withdrawing the catheter a small brown calculus was seen embedded in the wax. No doubt with the warmth of the body temperature the wax softened sufficiently to permit the calculus to become embedded during the few moments pressure was exerted when the obstruction was met. This surprising development caused the surgeon to remark to the patient "Well, you've used up all your luck."

DR. MUELLNER I wish to emphasize that uric acid stones are the most common of the nonopaque stones, and that they often are associated with an elevated blood uric acid level of 5 mg. per cent or higher. Determinations of the blood uric acid level, therefore, can be helpful when a presumed nonopaque stone is to be differentiated from conditions with which it is most likely to be confused, notably a ureteral tumor. Moreover, in uric acid calculus the elevated blood uric acid level is more apt to be due to hereditary hyperuricemia than to true clinical gout.

Dr. Ormond praised the usefulness of the wax-tipped catheter with which to search out the nonopaque stone and decried the ignorance which the newer generation of urologists seems to have of its use. This defection of the young urologists in itself suggests that their teachers are perhaps less enthusiastic in the use of the wax-tipped catheter than they used to be.

Dr. Moore has had particularly good luck in making the diagnosis and extracting a nonopaque calculus on the wax of his catheter all at once. I am wondering if my luck would be just the reverse of his, that is, the wax adhering to an embedded calculus, and the catheter coming away clean.

Dr. Locks referred to uric acid bladder stones, which I deliberately omitted from my paper. Here the problem is not serious. A patient who harbors uric acid calculi in his bladder will have symptoms, and sooner or later you have to do cystoscopy, and when you look into his bladder, you usually see the stones.



FIG 2 Right kidney showing enlarged, irregular tumor mass involving lower pole



FIG 3 Sagittal section of kidney showing size of tumor in relation to kidney

and arterioles. There is intimal sclerosis and the muscular layer is especially well-developed. In many places the vessels lie in the fat where they are surrounded by collars of immature muscle which streams out into the surrounding tissue. There are areas of necrosis and inflammation. The border between the tumor and

acid that a normal person has a reservoir of uric acid in the body fluids of about 1200 mg, which he referred to as a miscible pool. This pool is many times increased in the patient with gout. By this method Stetten showed that 50 to 70 per cent of this pool of uric acid is replaced by new uric acid each day. However, the mechanism by which uric acid is produced and destroyed has not been clarified and whether or not the rate of production of uric acid is greater in the patient with gout than in the normal person has not been established. Excretion of uric acid in the urine was not increased in patients with gout treated with isotopes in their series, however, these patients had the severe form of gout in which retention of uric acid due to renal damage is most likely.

The role of the kidney in gout has been a subject of controversy for many years. In 1863 Garrod⁷ theorized that in these cases retention of uric acid in the blood was due to some intrinsic defect of renal function which resulted in hyperuricemia and consequently in the recognized clinical evidences of gout. Because of the erroneous conclusion that a patient with gout does not excrete more uric acid than the normal person, this theory has lived throughout the years and is still held by many today. It cannot be accepted, however, for two reasons: 1) Renal disease does not necessarily co-exist with gout, and when it does, it is the end result and not the cause of the gout. 2) The type of renal disease that does appear to be due to gout is not one which would cause retention of uric acid in the blood stream.

It has been pointed out by Talbott and Coombs⁸ that if abnormal retention of uric acid in the blood existed in gout, there would have to be either increased tubular resorption or diminished glomerular filtration of uric acid. The former has never been adequately demonstrated in gout and the latter occurs only when there is advanced renal disease with retention of all nitrogenous products. The investigators⁸ were able to prove by comparative renal function tests on a series of patients with gout and on normal controls that the type of renal dysfunction seen in gout is tubular damage which results in diminished resorption of uric acid. From this it can be seen that in the early stages of gout before glomerular damage occurs there is increased excretion of uric acid in the urine associated with diminished tubular resorption.

It has also been pointed out by Friedman and Byers,⁹ Yu,¹⁰ Coombs and associates,¹¹ and Brochner-Mortensen¹² that renal failure to some degree will usually occur in time and that a significant number of these patients will die from renal insufficiency. Schnitzer and Richter³ reported that 31 per cent of 55 patients studied had chronic nephritis, and 22 per cent of the series of Hench and co-authors¹³ had this disease. In a review of 6 autopsy specimens Brown and

⁷ Garrod, A. B. *Nature and Treatment of Gout*. London: Walton and Maberly, 1863, 2nd ed., p. 618.

⁸ Talbott, J. H. and Coombs, F. S. J. *A. M. A.*, **110**, 1977-1982, 1935.

⁹ Friedman, M. and Byers, S. O. *Am. J. Med.*, **9**, 31-34, 1950.

¹⁰ Yu, T. F. *Am. J. Med.*, **9**, 799-817, 1950.

¹¹ Coombs, F. S., Pecora, I. J., Thorogood, L., Consolozio, W. A. and Talbott, J. H. *J. Clin. Invest.*, **19**, 525-535, 1940.

¹² Brochner-Mortensen, K. *Acta med. Scandinav.*, **106**, 81-107, 1941.

¹³ Hench, P. S., Vanzant, F. R. and Nomland, R. *Tr. A. Am. Physicians*, **43**, 217-227, 1928.

An uneventful postoperative course ensued, and the patient was discharged on the twelfth day subsequent to the nephrectomy. Repeated examinations during the past 30 months have disclosed no evidence of the tuberous sclerosis complex. To date her second pregnancy of five months gestation has been uneventful.

Case 2 P. H., a white man, 50 years of age, was admitted to the hospital January 19, 1949, in a semicomatose state. Five days prior to admission the patient had a temperature of 103°F, and complained of severe pain in abdomen following the taking of fluids.

The physical examination revealed a very dehydrated, apprehensive, and mentally confused patient. The temperature was 102.4°F. The palate was covered by a dried, brittle substance. The heart sounds were loud and rapid, and there

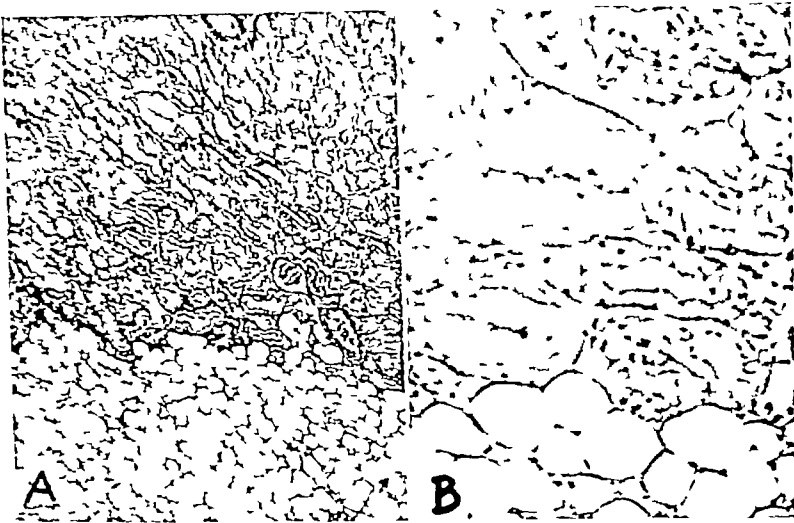


FIG. 5. A, hamartoma showing discrete tumor edge with apparent renal compression. Fat cells and renal tubules. $\times 300$. B, same area with compression of tubules. $\times 150$.

was a palpable thrill. Urinalysis showed specific gravity 1028, albumin 2 plus, occasional pus cells, a few red blood cells and rare hyaline cast. The clinical findings otherwise were within normal limits. Penicillin and streptomycin were administered for the rapidly progressive oral infection, which was believed to be a gangrenous stomatitis. The mental condition of the patient was considered to be a toxic psychosis. There were no symptoms, either in the present or past history referable to the genito-urinary tract. Death occurred on the seventh hospital day.

Postmortem diagnoses: acute, nonspecific, membranous stomatitis, etiology undetermined, terminal acute bronchitis, lobular pneumonia, generalized atherosclerosis, moderate cerebral cortical atrophy, considerable leptomeningeal fibrosis, adhesive pleural fibrosis, atrophy of left testis, atrophy of right kidney, and hamartoma of left kidney.

The right kidney was found to be atrophied and its entire lower half was covered by a fatty substance suggesting a nonfunctioning organ. The left kidney

the outer coats may predominate in the analysis and lead to the false conclusion that no uric acid is present. We have demonstrated this in some of our more recent patients with stones and believe that in some of the earlier analyses in this series the results may have been inaccurate because this possibility was not considered.

Of the 45 patients with proved stones in the series, 24 (53 per cent) were multiple and 14 (31 per cent) were bilateral. Ninety-three per cent were of renal origin and in 3 patients the stones were recovered from the bladder. However, the latter 3 all had obstruction of the vesical neck with partial urinary retention and their past history of renal colic suggested that the stones had originated in the kidney.

TABLE 1 *Incidence of urinary calculi in gout at Ochsner Clinic*

	CASES	PROVED CALCULI	
		Cases	%
Gout	324	45	13.89
General admissions	108,947	1337	1.23

Only 5 per cent of these calculi required surgical removal, this undoubtedly can be explained by the fact that uric acid calculi are usually small, round and smooth.

CORRELATION BETWEEN GOUT AND URINARY CALCULI

The importance of establishing a correlation, if possible, between gout and urinary calculi lies in the fact that adequate control of clinical manifestations of gout with resultant reduction in excretion of abnormal amounts of uric acid crystals in the urine will thereby retard further calculous formation and, in some instances, help to eradicate stones or soft masses of crystals already present. In order to establish this relationship fasting serum uric acid determinations should be done routinely and repeated frequently in patients with a history of stones, a consistent reading of above 5 mg. per 100 cc. is considered significant. Other possible stone-forming factors, such as hyperparathyroidism, cystinuria or xanthinuria, urinary infection, particularly of the urea-splitting variety, or evidence of stasis in the urinary tract as might be demonstrated by roentgenograms or cystoscopy should be ruled out. In determining the actual existence of gout one should consider not only the uric acid readings at the time of study but also any history of migratory arthritis and any familial history of gout. In this connection it is interesting to note that about 25 per cent of the relatives of a person with gout will have what is known as hereditary hyperuricemia and yet only a small percentage of these will ever exhibit clinical manifestations of gout.¹ It can be said, however, that hyperuricemia is associated with all cases of gout but there is not necessarily a direct relationship between the blood level of uric acid and the occurrence of an acute gouty attack. It should also be remembered that hyperuricemia, and consequently hyperexcretion of uric acid crystals in the urine, occurs not infrequently in patients with chronic myeloid leukemia, polycythemia vera, certain forms of hepatic disease and other rarer diseases. Therefore, it would

was present smooth muscle, numerous small and large thick-walled blood channels and fat cells of the adult type (fig 6)

COMMENT

Three cases of renal hamartoma were reviewed, one surgically diagnosed and the other two were incidental postmortem findings. The tuberous sclerosis complex was not associated with these 3 cases. However, isolated hamartomas of the kidney occur independently of tuberous sclerosis complex. The medullary "fibroma" is well-known. In addition, solitary lesions of the cortex have been reported under the name benign mixed tumor. They are generally small and are classified by whatever component is predominant, as hemangioma, lipoma, myoma, fibroma, etc. They are found mostly in adults, and except for infrequent hematuria they are symptomless.

As some patients have been known to develop clinical symptoms of tuberous sclerosis some years after the diagnosis of renal hamartoma, a detailed examination of the patient treated surgically was recently carried out. Thirty months following the diagnosis there is no evidence of the disease.

The lesion must be kept in mind in the differential diagnosis of renal neoplasms. Renal hamartoma is an interesting and rare tumor. Unless the lesion is large with associated spontaneous hemorrhage, it is unaccompanied by symptoms and consequently without clinical significance. The diagnosis may seem to be only of academic interest, nevertheless, the benign nature of the growth emphasizes its importance of prognosis.

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peated attacks of acute migratory arthritis usually in association with the urinary symptoms. This relationship, however, had never been considered significant. Cystoscopy and roentgenography had been done several times elsewhere but no definite diagnosis was made and no treatment given. Retrograde pyelograms made just before we saw him had shown no evidence of opaque calculi but did show a definite filling defect of the lower calyx and infundibulum of the right kidney (fig 1, A and B). This, coupled with the gross hematuria, seen at cystoscopy to originate from the right side only, had raised the possibility of tumor.

Gross examination of the urine at the Clinic showed the typical brick red sediment seen in cases of excessive uric acid excretion with evidence of blood as well, a trace of albumin and no infection. The sediment proved to be almost pure

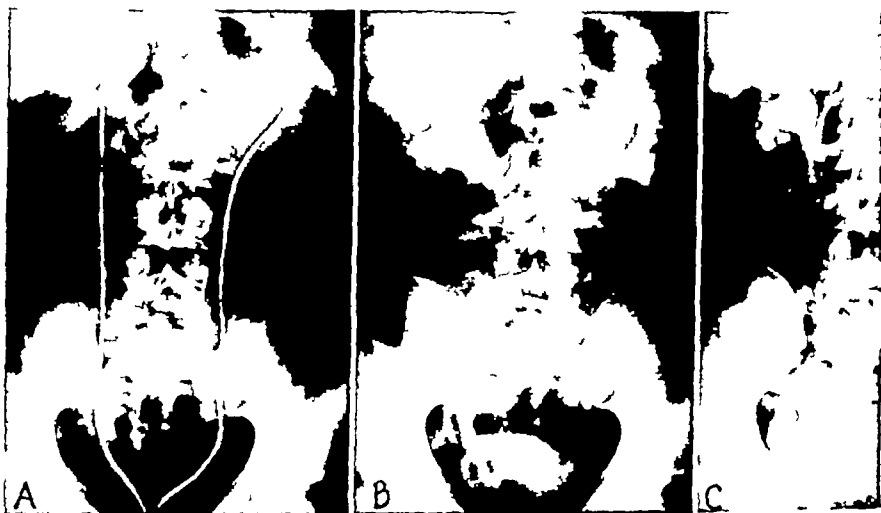


FIG 1. A, roentgenogram of the kidney, ureter and bladder with ureteral catheters in place showing no opaque bodies. B, retrograde pyelogram showing filling defect of lower calyx and infundibulum of right kidney. C, retrograde pyelogram 1 week after treatment showing absence of filling defect of right kidney.

uric acid crystals. Considerable impairment of renal function was demonstrated by a total phenolsulphonphthalein of 20 per cent in one hour and ten minutes and a blood urea nitrogen level of 33 mg. per 100 cc.

On the night of arrival a sudden attack of acute multiple arthritis developed which necessitated hospitalization. The next day the serum uric acid level was 15 mg. per 100 cc. Chemical analysis of the urinary sediment revealed pure uric acid. Plain roentgenograms of the urinary tract showed no evidence of opaque calculi. Since the previously noted filling defect could have been due to an accumulated mass of nonopaque uric acid crystals in the lower calyx of the right kidney, it was decided that pyelographic studies be deferred until the serum uric acid level had been reduced. Accordingly, he was given large daily doses of aspirin (60 gr. daily) to promote increased excretion of uric acid from the blood and sodium bicarbonate to alkalinize the urine and thereby increase the solubility of the crystals present in the urinary tract. Colchicine was given to relieve the arthritic symptoms. At the end of a week the patient was entirely comfortably

uric acid was 5.5 mg per cent. The infection was controlled with chloromycetin, and one week after the patient left the hospital he passed a uric acid stone.

Case 4 P. R., aged 46, BCH No. 1072739, was admitted July 6, 1942 and died July 15. He entered the hospital because of left flank pain of 1 day's duration, associated with vomiting. During the past year he had 3 previous attacks of renal colic and was said to have passed some stones. On examination, there was slight tenderness in the left costovertebral angle. Urine on admission was amber,

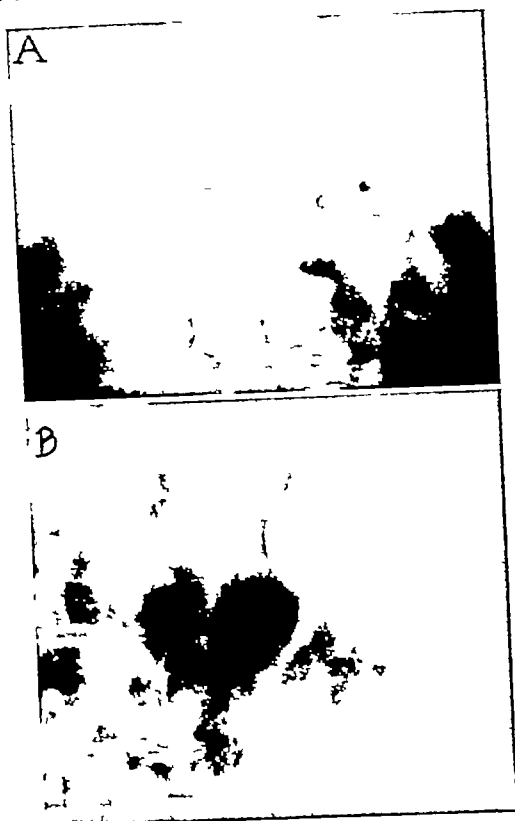


FIG 1 Patient complained of recurrent, painless, gross hematuria. A, excretory urogram. Note that diodrast was not excreted by left kidney. B, left retrograde pyelogram. Note negative shadows in pelvis, calyces and upper ureter suggestive of pyelitis and ureteritis cystica, papillary tumor of renal pelvis or nonopaque stones.

it contained a heavy trace of albumin, and the urinary sediment was loaded with red blood cells. The nonprotein nitrogen was 55 mg per cent but advanced rapidly to 91 mg per cent by July 10 and to 120 mg per cent by July 13. A plain x-ray was negative for stones. Excretory urography showed poor concentration and excretion of dye bilaterally. The retrograde pyelogram showed incomplete filling of both pelves and calyces but no evidence of stones. The cystoscopist was not aware that with his catheters he had passed by any ureteral stones. Following cystoscopy, oliguria developed and then anuria, which was interpreted by the house staff as being due to either reflex anuria as a result of the ureteral cath-

DISCUSSION

DR WILLIAM P HERBST (Washington, D C) Dr Kitttridge and Dr Downs have presented a very impressive investigative project concerning the relationship of gout to the incidence of uric acid urinary calculi, which should leave no doubt that people with gout are the victims of uric acid urinary calculi about 5 times as frequently as those without gout. Their treatment as described in detail in one of their cases is most interesting.

I should like to discuss some aspects of the metabolism of 1) stress, 2) administration of aspirin, and 3) the spa treatment. Selye has demonstrated that stress results in uric acid elaboration. Recently, Champy and Demay have demonstrated that the administration of salicylates and gentisic compounds produce the same reaction as ACTH insofar as its influence on lymphoid tissue and the reduction in cholesterol and vitamin C content of the adrenals are concerned. The breakdown of lymphoid cells elaborates amino acids which may be synthesized into uric acid.

(Slide) Here is a list of amino acids which depress or stimulate uric acid excretion: phenylacetic acid, benzoic acid, lactic acid, glycolic acid, acetoacetic acid, and ketosis depress the excretion of uric acid, and salicylic acid (aspirin), glycine, alanine, aspartic acid, glutamic acid, pyruvic acid, and P hydroxybenzoic acid and indirect stress stimulate its excretion.

Here we see that stress and aspirin both stimulate the excretion of uric acid. We also know that cortisone sometimes precipitates an acute episode of gout. Drs Kitttridge and Downs have experienced satisfactory results with aspirin, so even though some of our chemical data are confusing and suggestively unfavorable, why not use aspirin on a trial and failure basis?

The spa treatment of gravel and uric acid calculi involves the relief of stress, increased water intake and sodium bicarbonate. There are innumerable instances of the unmistakable relationship of periods of stress to uric acid calculus formation. It is of more than passing interest to note that the water at the celebrated spas at Vichy, France, has as its chief constituent sodium bicarbonate. The virtue of this water is attested to by the fact that over forty million bottles are sold yearly.

In closing this discussion, re-emphasis of the most important single factor of water intake is justifiable, inasmuch as this factor is, probably, the most important single known factor involved. At the same time we should again remind ourselves of the strong likelihood that the most important factors are unknown. They are the factors which would explain why 80 per cent of the patients with gout do not have uric acid calculi. These are the factors we should strive to discover.

DR W E KITTRIDGE: There are intrinsic renal changes that occur in chronic, long-continued and particularly severe forms of gout. There is tubular damage and the deposition of uric acid crystals along the tubules. That has been seen at autopsy. It makes you wonder that if the uric acid crystals were opaque, as

negative shadow, however, requires further differentiation. It may be due to an air bubble, to blood clot, to inspissated pus, to neoplasm, or to cystic degeneration of the mucous membrane.^{7 8}

Air bubbles in the retrograde pyelogram can, as a rule, be readily recognized, but an adherent small blood clot is not too easily differentiated from a nonopaque stone. This is true also of inspissated pus, tumor, or cystic mucosal disease.

To resolve this uncertainty the use of a wax-tipped catheter has been advocated. The presence of a stone is revealed by the characteristic scratch marks on the wax. While this method has some staunch advocates, many urologists have given it up because of its liability to false clues.

The suggestion has also been made to inject a few cubic centimeters of a 1 per cent solution of silver nitrate above and about the stone. The silver nitrate presumably coats the stone and gives it a mottled appearance on an x-ray film taken 12 hours later. Here again, silver nitrate may similarly coat noncalcareous material, and thus fail to resolve the question.

Air pyelograms also do not yield unequivocal and specific data. An ideal method to show up a nonopaque stone would consist of a substance which could safely be injected intravenously and which would then be excreted in the urine and combine with uric acid deposits to form a dense shadow. But as yet we do not possess such a substance.

Uncertainty of the existence, of the size, and of the location of a nonopaque stone is therefore an important clinical feature of this problem, and the urologist must be prepared to solve the problem on the basis of such uncertainty.

We have pointed out above that the single small uric acid stone is commonly being eliminated from a structurally normal urinary tract. Because the stone is apt to be small and the urinary tract normal in caliber and uninfected, it is logical to pursue a conservative management, whenever a presumptive diagnosis of nonopaque stone is made. A badly damaged urinary tract, as a result of an untreated uric acid stone, is rare and the consequences of a conservative attitude is therefore not fraught with disaster. An important exception to this is a bottled up severe infection of the urinary tract above the stone. An additional danger to conservative management is to mistake a tumor of the ureter or renal pelvis for a nonopaque stone. Here an elevated blood uric acid level can be a valuable aid in the differential diagnosis. If the blood uric acid is normal and the suspicion of tumor cannot be dispelled, the surgeon will be forced to explore the urinary tract for tumor after an initial period of observation and after re-evaluation of the findings.

We need not stress the difficulties which may beset the surgeon in search of a nonopaque stone which has not been localized with certainty preoperatively. Practically any maneuver designed to identify the stone immediately preoperatively may make matters worse. A catheter passed retrograde may push the stone up. If the catheter is pulled down, the stone may be dragged down with it, and in either case the new position of the stone may remain unknown to the surgeon.

⁷ Scott, W. W. *J. Urol.*, 50: 45-64, 1943.

⁸ Patch, F. S. *New Eng. J. Med.* 220: 979, 1939.

A MODIFICATION OF THE COUNCILL URETERAL STONE EXTRACTOR

JOHN P DAVIS

An instrument remarkably efficient for ensuring and extracting ureteral calculi was devised by removing all except two of the fixed wires from the Council stone extractor. The resulting instrument seemed to possess the advantages of the catheter loop without any of the difficulties encountered in the formation of the loop.

This modification was used as a pattern for a more delicate extractor developed by the author through the assistance of Mr. Frederick J. Wallace, President of the American Cystoscope Makers, Inc. This new instrument is small enough to pass readily through a 21F Brown-Bueger cystoscope (fig. 1).

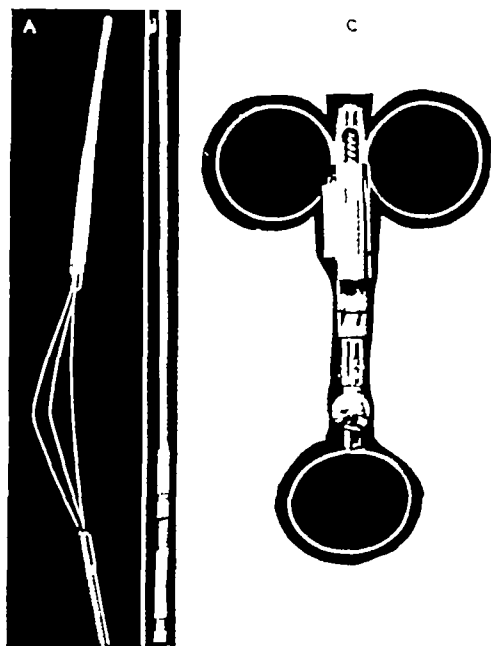


FIG. 1. Ureteral stone extractor. *A*, distal end; *B*, proximal end; *C*, detached handle.

The instrument possesses unusual ease of passage; it may be reinserted repeatedly at the same instrumentation; it has most of the advantages of the loop catheter without the difficulties associated with the formation of the loop, and if an x-ray shows that the stone has been missed, the instrument, because it is so small, may be pushed again above the stone, even though the cystoscope has been removed. The dangers in the use of an extractor of this type are well known to experienced cystoscopists.

The following technique has been found successful in the use of this instrument. Under anesthesia of choice, the stem of the instrument, handle detached, is passed through a 21F Brown-Bueger cystoscope above the level of the stone.

DISCUSSION

DR RUBIN H FLOCKS (Iowa City, Iowa) Dr Muellner has given us an excellent discussion of the unusual diagnostic and therapeutic difficulties associated with the management of renal and ureteral uric acid calculi. By means of concrete examples he emphasizes some of these.

The differential diagnosis between nonopaque stones and these other conditions which he mentioned, such as blood clot, tumor, desquamated epithelial cells, air bubbles, either originating in the urinary tract or introduced through ureteral catheters, ureteritis cystica or other conditions, may not be an easy one. Moreover, different types of calculi may be nonopaque, such as cystine, xanthine, certainly the sulfonamides, and some of the small calcium stones, and it is only by a complete urologic survey that the correct answer can be obtained in the individual case. Cystoscopy and excretory urography are indispensable.

Certainly, in doubtful cases with anuria, such as the first case which he mentioned this morning, the question of obstruction should be raised.

There are just a few points that I would like to emphasize. Although ordinarily, as he mentioned, uric acid calculi are small, they may be large, and associated with severe renal damage. In such cases the differential diagnosis may be a little more difficult than in the smaller ones, because of the size of the stone.

(Slide) This is an example of the largest kidney uric acid stone that I have seen. That patient had bilateral massive coral uric acid calculi, and was improved with operative procedure.

(Slide) This patient also had several large uric acid calculi in his kidney and another one in the midportion of the ureter.

In this particular individual, his main symptom was hematuria. The blood was seen coming from the right side, and in the process of making a differential diagnosis, we were misled by an examination which at times may be very helpful. In this particular case the Papanicolaou stain from the urine from the right side was positive. There were many peculiar cells there, and the attendant diagnosis of tumor of the kidney with an inflammation in the ureter was made. However, at operation, uric acid calculi were found.

(Slide) This is another case. You see the filling effect up in the left kidney, and the pyelogram on the right side, on the 9712. That turned out to be a mass of desquamated epithelial cells rather than uric acid stones.

In his discussion of nonopaque urinary stones, Dr Muellner has not mentioned some of the problems related to this type of calculi in the bladder. Nonopaque urinary calculi in the bladder, in my experience, occur about as frequently as they do in the upper urinary tract. Ordinarily they cannot be seen on the plain film, but in the air cystogram, or the opaque cystograms, they show up as negative filling effects, and must be differentiated from an enlarged prostate and bladder tumor, or from a blood clot in the bladder. Usually this is readily done by cystoscopic examination.

In our experience, some of these may be fairly large, and all the nonopaque stones that I have seen in the bladder, with very few exceptions, have proven to

MANAGEMENT OF URETERAL INJURIES

JOHN F. PATTON

From the Department of Surgery, Section on Urology, Washington University School of Medicine and Barnes Hospital, St. Louis, Mo

Injuries to the ureter in both war and civilian practice are comparatively rare and are less frequently encountered than injury to other levels of the urinary tract. The reports in the literature, however, do not reflect the true incidence since fewer than one hundred war wounds to the ureter have been reported to date and less than one thousand cases of injuries in civil practice. Many remain undetected and others unreported. Apparently stimulated by the last war, there has been an increasing number of articles dealing with the subject and, in general, the principles of management are well defined. These include, though not necessarily in their order of application, 1) early recognition, 2) adequate drainage in the presence or prevention of extravasation, 3) diversion of the urinary stream above the point of injury for protection of the kidney, 4) repair of the defect. These apply regardless of whether the injury is due to a gunshot or shell fragment or the result of some form of surgical trauma. The circumstances of the injury and the causative agent, however, may influence the immediate course of procedure, and each case presents an individual problem. The primary consideration in all instances should be the preservation of the kidney with ultimate restoration of the continuity of the urinary tract to as nearly the normal state as possible, subject of course to first consideration of the individual's life as a whole.

WAR INJURIES

Although the principles involved remain the same, certain aspects of war injuries deserve separate discussion. War injuries of the ureter result from gunshot or shell fragment in which the ureter is either partially or completely severed, and are usually accompanied by more serious injury to the abdominal viscera. Robinson, et al. reported 25 wounds of the ureter and only 2 cases ruled to have injury to other organs. In the presence of severe abdominal wounds, injury to the ureter becomes of secondary importance, and as a result they are frequently overlooked. It may be said that in any case of penetrating wound of the abdomen, particularly if the point of entrance is in the flank or if on abdominal exploration the foreign body is found to penetrate the posterior peritoneum, ureteral injury should be suspected. If the time element is important and prolonging the surgery to determine the existence of a ureteral injury would appear hazardous to the patient's life, the retroperitoneal space should be drained on suspicion. This can be done through a small muscle-splitting incision or even a simple stab wound. While urine from a ruptured ureter draining into the retroperitoneal space may not be of serious consequence, extravasation into the peritoneal cavity may be fatal.

Even if the injury to the ureter is recognized, the condition of the patient

Read at annual meeting, American Association of Genito-Urinary Surgeons, St. Louis, Mo., May 16, 1951.

cells, air bubbles, ureteritis cystica and this differential diagnosis is greatly aided by a thorough study of the patient, his history, the character of his urine (particularly the pH), the nature of the crystals, the nature of the cytology of the urine and by repeated excretory and retrograde studies. Excretory urography is indispensable and is of tremendous aid in the solution of problems connected with nonopaque urinary tract stone. Moreover, urinary tract stone which is nonopaque and is in the bladder is practically always a uric acid stone and these stones are extremely hard. They are, therefore not usually as amenable to litholapaxy as stones of other compositions (except oxalate) of similar size.

DR RICHARD W. SATTERTHWAITE (Ancon, Canal Zone). I wish to mention two points. 1) The use of an excretory urogram during or immediately after the period of acute pain is an effective and simple means of detecting at once nonopaque ureteral obstruction. Although this was mentioned years ago by Drs. Braasch and Wesson, and many others, it does no harm to re-emphasize this point as a means of differential diagnosis for the general surgeon whom, it seems, presents the urologist too often with a fresh appendiceal scar and a nonopaque ureteral calculus.

2) Our experimental work in uric acid metabolism during the last 18 months was stimulated by two clinical observations: a) the occurrence of a large number of uric acid stones under unusual conditions in a large series of patients, and b) the observation that in some cases of uremia there is a high blood sugar, even though there had been no prior history of diabetes.

In our studies in the Dalmatian dog, we have used ACTH, and high protein diets, and changes in the fluid intake. Although we have not produced what we consider uric acid calculi, it has been possible to show that ACTH, or stress, produces a marked rise in the urinary uric acid which may be more than treble the normal level. We have produced aggregations of uric acid crystals, but no definite calculi, or obstruction of the ureter. We mention this work since we feel that stress may play a part in the formation of some types of uric acid calculi.

DR JOHN K. ORMOND (Detroit, Mich). I want to call your attention to a diagnostic procedure that seems to have gone into disuse in the last few years, namely the use of the wax tipped bougie.

Twenty-five years ago it would not have been necessary to call attention to this. I have been very much surprised to find that a great many—particularly among the younger men—have never heard of this procedure, and don't know anything about it.

It is very simple. In our clinic we always have a small bottle of beeswax on hand. We heat it over a spirit lamp and dip the bougie or catheter in the wax. We then pass it through the cystoscope into the bladder. As it enters the bladder, we deflect it downward, so it doesn't catch in the end of the cystoscope. Then it is passed up the ureter. We try to have the wax tip as large as will enter the orifice. If it meets an obstruction, it is twisted, and when brought out if the end is chewed to pieces, the diagnosis of a stone is made. If it passes up the ureter one can usually feel the place where the obstruction is, and if the bougie is twisted as it is withdrawn a spiral scratch on the side of the wax may be found.

It does not take much practice to learn to differentiate the straight and shallow scratches caused by the passage through the instrument, from the deeper and

orifices plainly in view, so catheters were passed to rule out possible ureteral injury. The right ureter was found to be ligated 4 cm. from the bladder and was of approximately 45 minutes' duration. Deligation was carried out, a ureteral catheter left in place and the bladder defect repaired with good end result. The ureter distorted by closely approximated sutures may be handled in a similar way. If the ureter has been partially severed, a splinting catheter should be all that is necessary. If crushed or completely divided, re-anastomosis or transplantation to the bladder seems the preferred choice. Extensive loss of ureter, though rare, may necessitate consideration of such procedures as uretero-intestinal anastomosis, cutaneous ureterostomy or transuretero-ureteral anastomosis as devised by Higgins. The latter has been successfully applied by both Moore and Smith. Ligation of the ureter with the purpose of producing hydronephrotic atrophy of the kidney is to be condemned and is permissible only under the most urgent circumstances. If the condition of the patient does not permit the time required for definitive surgical correction, a temporary nephrostomy or ureterostomy is the safest course.

Unfortunately, the injury is usually not evident until sometime during the postoperative period. Bilateral ligation produces immediate and grave symptoms with anuria and demands prompt intervention by deligation or bilateral nephrostomy. The postoperative course in the presence of unilateral injury is usually a stormy one although there may be no symptoms to direct attention to the kidney. Renal pain may be expected in only approximately 50 per cent of the cases. Oliguria, unusual fever or renal tenderness should make one suspicious and warrants early investigation. A urinary fistula is often the first positive sign and was present in 54 per cent of the 35 cases referred to previously, occurring most frequently between the fourth and eighth day. In one case the fistula developed as late as 21 days.

Attempts at correction of the injury during the early postoperative period may be difficult or even hazardous, and if infection has intervened, would seem contraindicated. Simple deligation over a splinting catheter may be considered feasible in certain instances but, to be successful, must be performed early before the ureter has undergone excessive damage. Moore reports a case of successful bilateral deligation on the third postoperative day. Each case presents an individual problem and it may be said that, in general, temporary nephrostomy remains the safest course of procedure.

URETERAL ANASTOMOSIS

As stated previously, re-anastomosis of the ureter or reimplantation to the bladder is the method of choice in restoring the continuity of the urinary tract, and likewise they provide a nearer approach to the normal state. Re-anastomosis is generally accepted as the preferred method of repair in dealing with high ureteral injuries and should be equally applicable in most low injuries. The difficulty is usually in isolating the distal segment, but one should be able to accomplish this by careful dissection and the use of a large caliber ureteral catheter inserted from the bladder side to aid in its location. The majority of surgical injuries to

THE ROLE OF GOUT IN THE FORMATION OF URINARY CALCULI

W E KITTREDGE AND RALPH DOWNS

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Recent experience in the management of certain patients with urinary calculi has impressed us with the fact that there must at times be a definite correlation between this condition and gout. Although many urologists recognize the importance of determinations of serum uric acid levels in the diagnostic study of patients with urinary calculi, a review of the literature reveals relatively little emphasis on the correlation between gout or hyperuricemia and the appearance of uric acid calculi. Many believe that a rather high incidence of urinary calculi is associated with gout but Joly,¹ among others,^{2,3} considered the occurrence of nephrolithiasis in gout to be entirely coincidental. In an attempt to evaluate the possible relationship between urinary calculi and gout, we analyzed 324 cases of patients with proved gout admitted to the Ochsner Clinic during the 9 year period ending December 31, 1950.

HISTORICAL

Uric acid calculi have figured prominently in the history of stones. The oldest stone in present day collections contains a uric acid nucleus. It was recovered from an Egyptian mummy who died 7,000 years ago. Also, it was from chemical analysis of a vesical calculus that Scheele⁴ in 1776 was first able to identify uric acid in the human body.

ETIOLOGY AND PATHOLOGY

The etiology of gout is not known. The disease is considered to be a disorder of purine metabolism manifested clinically by recurrent migratory arthritis, hyperuricemia and frequently renal complications in the later stages. The metabolism of uric acid is not as yet thoroughly understood. It is the end product of purine metabolism. It appears in the body from both endogenous and exogenous sources and is for the most part excreted by the kidney. The serum uric acid level is usually elevated in patients with gout, and Bauer⁵ believes that in all patients with gout at some time the serum uric acid level will be abnormally high. Correlation between the level of serum uric acid, precipitation of a gouty attack of arthritis and excretion of uric acid by the kidneys are indefinite.

Stetten⁶ recently demonstrated by the intravenous injection of isotopic uric

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¹Joly, J. S. *Stone and Calculous Disease of the Urinary Organs*. St. Louis: C. V. Mosby, 1940.

²Reich, N. *Internat. Clin.* 4: 232-280, 1939.

³Schnitzer, M. A. and Richter, A. B. *Am. J. Med. Sc.* 192: 241-252, 1936.

⁴Scheele, K. W. Cited by Levene, P. A. and Bass, L. W. *Nucleic Acids*. New York: Chem. Catalog Co., 1931.

⁵Bauer, W. in Duncan, G. G. *Diseases of Metabolism*, Philadelphia: W. B. Saunders Co., 1947.

⁶Stetten, DeWitt. *Am. J. Med.* 9: 799-817, 1950.

could be prepared for definitive treatment. A drain was also placed through the cervical canal to improve drainage. On October 25, six weeks after the original operation, a uretero-ureterostomy was performed. The proximal ureter was exposed extraperitoneally and dissected free with ease. The distal segment was bound by dense adhesions but when isolated was found to be of sufficient length to warrant a re-anastomosis. An end-to-end approximation was performed using 0000 chromic catgut and a polyethylene tube of approximately 10l was inserted as a splint and brought out through the urethra. The wound was closed with drainage and a urethral catheter was placed in the bladder alongside the polyethylene tube. The nephrostomy tube was removed at this time. She had an uneventful postoperative course and both the polyethylene tube and the urethral catheter were removed on the eighth postoperative day, at which time



FIG 1 A, preoperative excretory urogram showing degree of right hydronephrosis. B, retrograde ureterogram showing point of injury and extravasation of dye. C, retrograde ureteropyelogram 13 days postoperative. D, retrograde ureteropyelogram after 1½ months showing regression of previous hydronephrosis.

the urine was clear and free of infection. There was no evidence of leakage at the site of anastomosis following removal of the tube. On the thirteenth postoperative day a No. 10 bulb catheter was passed up the right ureter without difficulty and a ureteropyelogram appeared satisfactory (fig. 1, C). She was discharged on the following day. A ureteropyelogram after 4½ months shows an essentially normal kidney with evidence of regression of the previous moderate hydronephrosis (fig. 1, D). A No. 8 bulb catheter passed up the ureter easily. The final result in this case can only be determined by a later follow-up.

RE-IMPLANTATION TO THE BLADDER

If the distal segment of ureter is not of sufficient length to permit re-anastomosis, re-implantation of the proximal ureter into the bladder is the method of choice. Numerous techniques have been proposed for re-implantation and it is generally agreed that the preferred site is the base or fixed portion of the bladder.

I wish to present a late follow-up of a case previously reported and which to the best of my knowledge is the first instance of re-implantation of the ureter into the bladder through the normal intramural bed.

Mallory¹⁴ indicated that 2 patients had died of "uremia" and that all 6 had had clinical evidence of renal failure before death

The pathologic alterations in the kidney, as has been shown by Brown and Mallory,¹⁴ are due to 1) a collection of urate crystals in the collecting tubules, which causes slough of the tubular epithelium with eventual necrosis of the tubules, and 2) varying degrees of nephrosclerosis, which is due to the generalized changes in the blood vessels so prominent in gout. The former process is thought to be the primary renal lesion in gout producing diminished resorption of uric acid crystals and consequently increased excretion of uric acid and urates in the urine as well as collection of crystals in the tubules. The nephrosclerosis occurs in the later stages of gout and eventually produces glomerular damage and retention of uric acid as well as other nitrogenous products. In the autopsies reported by Brown and Mallory¹⁴ the proximal tubules were clogged with uric acid crystals, similar to the pathologic alterations seen in the nephrocalcinosis of hyperparathyroidism. Undoubtedly, if these uric acid crystals were radio-opaque, as is calcium, the roentgenogram would be similar to that seen in nephrocalcinosis. It is interesting to note here that the mechanism of calculous formation in gout may be similar to that occurring in hyperparathyroidism, in that a similar destructive process occurs in the tubules with resultant increased crystalluria.

ANALYSIS OF CASES

Thirty-seven per cent of the 324 patients in our series had had a complete urologic study and in the remaining 63 per cent the history of urinary calculus was either established or ruled out by the medical history taken on admission. In 45 patients (14 per cent) a stone had actually been recovered or demonstrated roentgenographically prior to admission. An additional 11 patients (3 per cent) gave a typical history of renal colic, although stones were neither recovered nor demonstrated roentgenographically. If these latter cases were included, the incidence of calculi in patients with gout would be 17.28 per cent as compared with an average incidence of 1.23 per cent of urinary calculi occurring among 108,947 general admissions to the Clinic during the same period (table 1). All our patients were males. It is generally agreed that 95 per cent of all cases of gout occur in males.

Of the 45 definitely proved cases of stone occurring in association with gout, we were able to obtain calculi from 14 for analysis. Nine (64 per cent) of the stones were composed of uric acid, two-thirds of these were not demonstrable roentgenographically prior to their passage. The remaining were not of uric acid composition. This emphasizes the fact that any patient with a metabolic disorder, whether it be gout, hyperparathyroidism or any other similar condition, may still form urinary calculi as a result of entirely unrelated causes. It must also be borne in mind, however, that a stone may have a nucleus of uric acid, which later becomes coated with some other substance, such as calcium oxalate, or in the presence of infection, with the triple phosphates. Unless, in the chemical analysis of the stone, particular care is taken to isolate the nucleus for separate analysis,

¹⁴ Brown, J. and Mallory, G. K. *New England J. Med.*, 243: 325-329, 1950.

PLASTIC SURGERY OF THE URETER IN CHILDREN

JOHN K. ORMOND AND ROBERT W. OSBORN

From the Henry Ford Hospital, Detroit, Mich

In spite of the acceptance of the principle of conservation of renal function and the realization that the younger the patient the more important is conservation, as we review the literature and talk with other urologists we find that many have never attempted plastic surgery on the ureter in children and others give discouraging reports of their results.

We have had the opportunity to perform plastic operations at the upper end of the ureter in seven children, and at the lower end in five, and have been able to follow them long enough to judge of their efficacy.

The problems presented at the lower end of the ureter differ in one very important feature from those presented by the upper end, namely that of reflux. At the upper end the problems are those of organic obstruction and infection, while at the lower end they are those not only of obstruction (either organic or functional) and infection, but also of reflux. The elimination of obstruction at the cost of producing reflux yields only partial and temporary relief. In these cases we are not dealing with normal ureters in which the normal activity of the ureter plays at least some role in preventing reflux, even if that role be subordinate to that of the valve action of the intramural ureter. This may be illustrated by those cases in which ureters are reimplanted into the bladder following segmental resection for carcinoma. Many of these show no reflux though it is probable that any valve action produced must be incomplete. In the cases in which plastic operation at the lower end of the ureter is indicated, we are nearly always dealing with dilated and infected ureters which have lost all possibility of muscular activity and have become mere inert tubes.

In all cases there is some diminution of renal function and some dilatation of the pelvis or ureter or both. We cannot expect complete restoration to normal, but we can hope for the halting of the progress of functional deterioration, and even for some restoration of function, and for prevention of further anatomical dilatation. We would, therefore, estimate the success or failure of operation in any case by the degree in which it had 1) relieved symptoms, 2) eliminated or prevented infection, 3) halted the progress of functional deterioration and 4) halted the progress of anatomical change.

The first group of cases we are presenting consists of 7 patients subjected to plastic operations at the upper end of the ureter.

Case 1 Henry Ford Hospital No. 189884, a 9 year old boy had recurring attacks of fever accompanied by pyuria, failure to gain properly, and slower development than his twin brother. Excretory and retrograde pyelograms showed marked hydronephrosis on the left (fig. 1, 1). A plastic operation was done on the ureteropelvic junction, a splinting catheter being used and removed in about two weeks. Two months postoperatively dilatation of the ureter was done. Pyuria

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seem that in these diseases, as in gout, arthritic symptoms and calculous formation might occur,¹⁵ although Best and Taylor¹⁶ do not think this possible

TREATMENT

In the control of gout itself a low purine diet should be employed to lessen the excretion of urates in the urine. It has often been noted that exogenous uric acid does not play the major role in uric acid excretion and that the final metabolism is more important, but it seems logical to avoid adding an excess of high purine foods to a metabolic process that is already inadequate or inefficient. One should also alkalinize the urine by administration of sodium bicarbonate in dosage up to 40 gr 4 times a day in order to maintain a pH of 7, since uric acid crystals are soluble in an alkaline medium. Appropriate drugs should be given to bring about as great a reduction as possible in the blood uric acid level with a view to eventual reduction in the urinary concentration of uric acid crystals. Among the best of these in present usage is aspirin in dosages up to 6 gm daily, since this drug acts as a uric acid diuretic in this dosage. Less than 4 gm daily may cause retention of uric acid in the blood stream with consequent elevation of the serum uric acid level. The preventive treatment of gout by continued administration of aspirin has been of questionable value but has proved efficient in some instances.

Colchicine is the drug of choice in the treatment of acute attacks of gouty arthritis. Its action is not understood but it is known not to cause hyperexcretion of uric acid in the urine. The usual dosage is 0.5 mg three times daily. According to Bauer and Klemperer,¹⁷ cinchophen will produce hyperexcretion of uric acid in the urine but should not be used because of its toxicity. Cortisone or ACTH, which also produces hyperexcretion of uric acid in the urine, can be employed in cases of gout that have proved resistant to other forms of treatment. The dosage is not as yet well established but customarily 150 to 200 mg daily in 4 divided doses is given. ACTH, however, can precipitate an acute attack of gouty arthritis¹⁸ and therefore should not be used routinely. Other important general therapeutic measures include adequate hydration, adequate vitamin intake, treatment of any urinary infection present and correction of any obstructive lesion in the urinary tract which could cause stasis of urine.

The following case well illustrates both the relationship of gout to the formation of urinary calculi and the results that can be accomplished by the control and management of gout associated with uric acid crystalluria.

CASE REPORT

R. E. P., a single white man, aged 26 years, had had recurrent attacks of renal colic on the right side associated with hematuria usually lasting 3 to 4 days and often accompanied by the passage of soft brown sandy material in the urine. He had no symptoms between attacks. Since the age of 7 years he had also had re-

¹⁵ Hyman, T. H. *An Integrated Practice of Medicine*. Philadelphia: W. B. Saunders, 1947, p. 231.

¹⁶ Best, C. H. and Taylor, N. B. *Physiological Basis of Medical Practice*. Baltimore: Williams & Wilkins, 1950, 5th ed.

¹⁷ Bauer, W. and Klemperer, F. *New England J. Med.* 231: 681-685, 1944.

¹⁸ Hollman, L. *Science* 109: 289, 1949.

aberrant vessel was found crossing the ureteropelvic junction and a stricture of the ureteropelvic junction. The stricture was excised and reanastomosis of the ureter performed on the other side of the vessel, which was not sectioned. A splinting catheter and nephrostomy were used.

Pyuria persisted for several months and then ceased. For the past 3 years the patient has had no trouble, has had perfect health and has grown and developed normally. Pyelograms 6 months postoperative showed little change in the pelvis, or in function.

In this case after a few months there was relief of symptoms and infection, though no improvement functionally or anatomically.

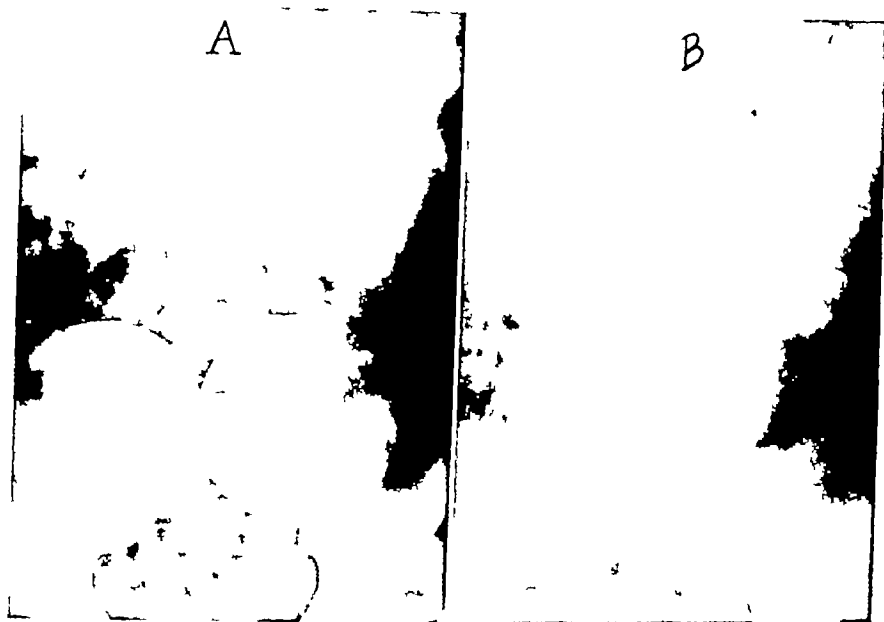


FIG. 2

Case 4. Henry Ford Hospital No. 423846, poorly nourished 1½ month old boy had failed to gain in spite of a good feeding schedule and had recurrent episodes of vomiting. On cystoscopy, the right ureter could not be located and the catheter could be passed only 2 cm. on the left.

A congenital narrowing was found of the upper 2 cm. of the ureter with consequent hydronephrosis. The narrowed section of the ureter was excised and the ureter re-implanted into the pelvis, the ureter being splinted, and nephrostomy done. Two weeks later the left kidney was explored. A rudimentary kidney was found and removed. Postoperatively the feeding problem was quite troublesome for a few months after which he gained satisfactorily. A phenolsulfonphthalein test 4 months postoperative showed 12 per cent output in 2 hours. Two years after operation urinalysis showed no pus. Five years after operation the phenol sulfonphthalein test showed 25 per cent in 2 hours. An excretory urogram was unsatisfactory.

and the urine had become crystal clear, no longer showing any uric acid crystals on microscopic examination of the centrifuged sediment. The serum uric acid level had dropped to 4.2 and the blood urea nitrogen to 19 mg per 100 cc. At that time retrograde pyelograms showed no further evidence of a filling defect in the right kidney, this ruled out the possibility of tumor and confirmed the fact that the previous defect had been due entirely to the presence of a mass of uric acid crystals in the lower calyx and infundibulum (fig. 1, C).

The patient was allowed to go home with instructions to continue taking aspirin in dosages of 45 gr daily for 1 week of each month and sodium bicarbonate daily, and to employ a low purine diet. He also was to take colchicine intermittently, 0.5 mg tablets daily for its possible value in preventing arthritic attacks as well as for its usefulness in acute attacks.

In the year which has now passed since the patient was first seen by us he has had only two mild attacks of renal colic and these occurred when he neglected to follow the prescribed regimen. He has had no further attacks of arthritis and has not seen any grossly recognizable evidence of uric acid crystalluria.

SUMMARY

Our experience has shown that there is often a definite correlation between the clinical manifestations of gout and the occurrence of urinary calculi of uric acid composition. Of 324 patients with proved gout admitted to the Ochsner Clinic during a 9 year period, between 14 and 17 per cent had a definite history of urinary calculi as compared with an average incidence of 1.23 per cent among general admissions to the Clinic.

The renal pathologic change which occurs in gout is primarily one of tubular damage, which is conducive to increased uric acid excretion and thereby calculous formation. Elevation of the serum uric acid level in gout is not due primarily to renal dysfunction except in the event of advanced nephrosclerosis, in which all nitrogenous products are retained. In the early stages of gout, even in the presence of renal damage, excretion of abnormally large amounts of uric acid and urate crystals is not hindered.

The importance of establishing the relationship between the clinical manifestations of gout and urinary calculus formation lies in the fact that control of the gout will frequently retard or prevent further calculous formation. A case is presented which illustrates both the relationship of gout to calculous formation and the results which can be accomplished by control of the gout.

tomy tube, both of which were removed by the fourteenth day. One month post operative he was free from symptoms and his urine was clear, and from then on his energy and appetite improved. This improvement has continued and he has become very active. Excretory urograms 3 years after operation showed slight enlargement of the left pelvis, with good drainage and normal calyces. The urine has remained clear (fig. 3, B).

Case 7 Henry Ford Hospital No. 580735, an 8 year old boy was brought to our attention because of recurring attacks of left flank pain for 1 year. Occasionally he would vomit during these attacks but he had no urinary symptoms. He was a well nourished boy with no positive physical findings, and his urine showed only an occasional pus cell. Pyelograms showed a fairly large hydronephrosis on the left with obstruction at the ureteropelvic junction. At operation a congenital stricture was found $1\frac{1}{2}$ inches below the ureteropelvic junction, and this was treated by intubated ureterotomy, using a splinting catheter and nephrostomy drainage. The splinting catheter disappeared into the wound, and was removed through a left McBurney incision at 5 weeks postoperative. A week later his urine was clear and has remained so. There has been no recurrence of the abdominal or flank pain, and he has been very active. Excretory urograms 6 months after operation show persisting hydronephrosis with fair function.

We have reported 7 cases of upper ureteral obstruction in children treated by various plastic operations. In no instance has subsequent nephrectomy been required. In 6 cases symptomatic relief has resulted, and the progression of renal deterioration has been halted. In one instance (case 3) relief of symptoms did not occur for several months and may have been independent of the treatment to the urinary tract. In this case moreover, we are not able to determine to what extent renal function has been benefited.

As we review these 7 cases we believe we are justified in claiming success in six and it is difficult to consider the other one a failure.

We will now report on 5 cases of plastic operation at the lower end of the ureter: one for congenital obstruction at the lower end of the ureter, two for ureterocoele, and two for what we considered to be cases of congenital megalo-ureter.

Case 8 Henry Ford Hospital No. 279715, an 8 week old boy was seen because of an enlarging abdomen with palpable masses in the flanks, loss in weight, and an elevation of the blood nonprotein nitrogen. Cystoscopy was not accomplished. Bilateral nephrostomies were done for infected hydronephrosis and his condition improved considerably. Later the enlarged and tortuous ureters were straightened by excising their upper ends. A suprapubic exploration was then done and a probe could not be passed into bladder from either ureter. Lateral incisions were done between the ureters and the bladder. He continued on suprapubic drainage throughout his life, gradually going downhill until his death shortly before his tenth birthday.

Case 9 Henry Ford Hospital No. 528176, a $5\frac{1}{2}$ month old girl had had recurring episodes of urinary infection since birth. Excretory urograms showed a normal left pyelogram, calyceal dilatation on the right, and a globular, radiolucent area in the bladder. The latter proved to be a ureterocoele at cystoscopy and was later seen to protrude through the urethral orifice. At operation the golf ball sized

calcium, perhaps you would get the same x-ray picture sometimes in gout that you get in nephrocalcinosis

Years ago the workers all believed that the renal changes which occurred in gout could not cause retention of uric acid crystals in the blood, and therefore that the kidney itself was not responsible for gout. That was true and is still true, in the sense that tubular damage will naturally cause greater excretion and less resorption of uric acid and actually creates more of the urinary picture, the urinary crystalluria, that we actually do see in cases that have an elevated blood serum uric acid.

In the final stages of gout however where complete breakdown of the kidney occurs, with deficiency of glomerular filtration, then and only then do you get an increase in the blood uric acid due to the fact that the kidneys cannot excrete their usual quota of uric acid.

In connection with ACTH and cortisone, I just want to say that some of the experts, at least, who treat a good deal of gout, believe that those two drugs should be reserved for difficult cases. They think it can help some, but they also know it actually can precipitate an attack of gout. That is why they are a little slow to use it.

Aspirin, curiously enough, can actually cause retention of uric acid, rather than uric acid diuresis, if used in doses too small. So you must remember that if you are going to use aspirin, you must use 60 gr. a day.

brile attacks and persistent pyuria resistant to a variety of antibiotics and chemotherapeutic agents. Initial pyelograms showed bilateral hydronephrosis and hydro-ureter, most marked on the left. A ribbon of tissue was removed from the

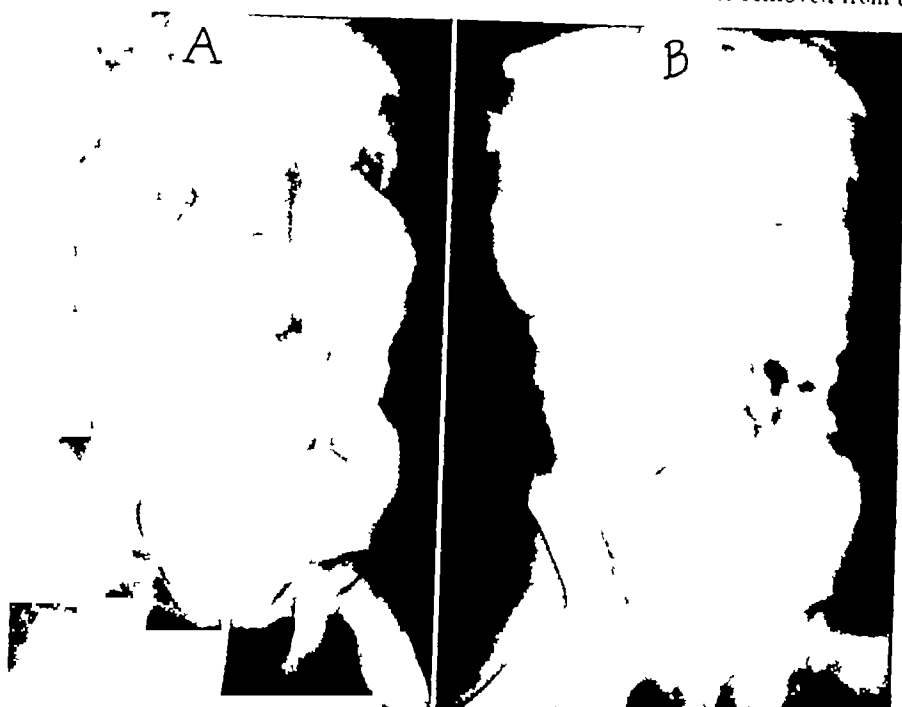


FIG. 4

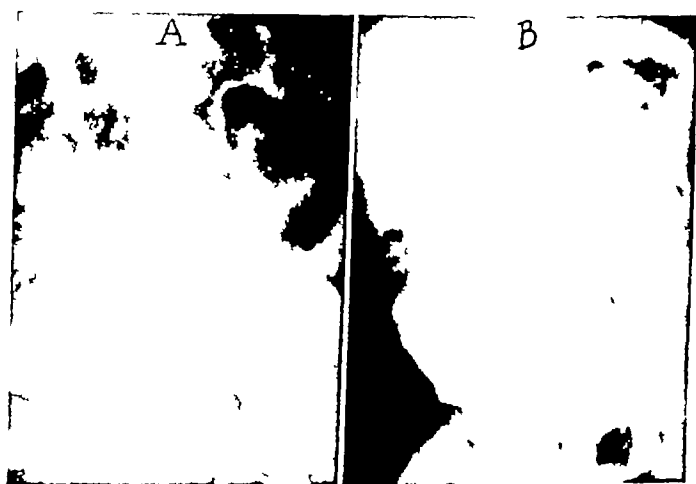


FIG. 5

left ureter is described in case 11. Three months later pyelograms and cystogram showed some reflux on the left, but apparent improvement in the dilatation (fig. 5, 4). Since the process on the right side seemed to be progressing, a similar operation was done on it. A cystogram taken 4 months postoperative shows bi-

The cystoscope is then removed, leaving the stem in place. The handle is attached to the stem and the snare is opened to the desired width. The instrument is then slowly withdrawn. Increase on the drag usually indicates that the stone has been engaged. This may be confirmed by an x-ray of the kidneys, ureters and bladder. If the snare has slipped below the level of the stone and failed to engage it, the instrument is pushed back up the ureter without re-inserting the cystoscope, until the snare again lies above the level of the stone. The snare is re-opened and the instrument slowly extracted. With careful and gentle traction, the stone is usually engaged and removed by its retention in the wire mesh.

This instrument will find its greatest usefulness in the lower third of the ureter. It has not been used to extract a stone higher than the third transverse lumbar process.

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DISCUSSION

DR MEREDITH CAMPBELL (New York, N Y) The splendid presentation of Drs Ormond and Osborne vividly indicates the strides which have been made in the conservative surgical treatment of ureteral disease in the young, and notably obstructions. Because of the remarkably favorable reversibility of the renal damage and disease in many infants and children following the establishment of free drainage and adequate urinary antisepsis, we may hopefully attempt conservative ureteral surgery in a large number of patients in this age group. Yet such procedures applied to adults comparably afflicted would be doomed to certain failure. Moreover, the end results, as cited by Drs Ormond and Osborne, indicate that some patients are relieved, temporarily at least, though in some instances the results are unsatisfactory, and that only by treating the many can we cure the few.

Although we have employed the Foley-Schwytzer Y-plasty in the treatment of ureteropelvic obstruction presumably congenital in many infants and children, the results have sometimes left considerable to be desired. Yet, in some cases the relief of obstruction has been complete with corresponding restoration of renal function. In three young patients the procedure was carried out on the only kidney, and in our work resection of the greatly redundant pelvis is generally performed in addition to the ureteropelvioplasty.

Some of these pelvic outlet strictures extend down the ureter for two or more centimeters and in these cases the longitudinal incision of the stricture-bearing area with the T-tube implantation technique of Davis has been amazingly successful, leaving the pelvic outlet and upper ureter of much wider than normal caliber. This procedure was most successfully employed in the treatment of a longitudinal filiform stricture of the body of the ureter of an only kidney in a 3 year-old girl with chronic pyuria, recurrent hematuria, and complete urinary incontinence. Although not included in the essay just given, these strictures of the body of the ureter have offered us the greatest difficulties in surgical therapy. Examination of the 3 year-old girl just cited disclosed bilateral ureteral ectopy, the right ureter terminating in a pinpoint size orifice in the midurethra. Back-pressure destruction and infection demanded right nephroureterectomy. On the left the ureter opened ectopic at the vesical outlet and in the adjacent urethra, the orifice being elongated and crescentic. The longitudinal stricture, presumably congenital, at the junction of the middle and lower thirds of the left ureter would just permit the passage of a 3F catheter but a 11 w was prohibited. The ureter and pelvis above were dilated. The stricture-bearing area was longitudinally incised for a distance of 4 cm and an 18F T-tube was left indwelling for 3 weeks, one arm passing to the lower ureter, the other to the renal pelvis. Eighteen months later, a 12F bulb could be passed freely from the bladder to the renal pelvis.

Finally in the treatment of the left ectopic ureteral orifice in this case, I used a trick suggested by Nesbit a few years ago. The root of the ectopic ureter was

may not permit initial repair of the defect and drainage with exteriorization of the proximal end of the ureter, nephrostomy or ureterostomy may be necessary as a temporary measure. With adequate drainage and diversion of the urine, one can safely wait until such time as the patient's condition will permit proper investigation and definitive treatment. If initial repair of the ureter is feasible, an end-to-end anastomosis over a splinting catheter, or re-implantation into the bladder is the method of choice. Excessive loss of ureter, necessitating nephrectomy or resort to transplantation procedures, is infrequent.

Ureteral injuries, unfortunately, are usually recognized only after a urinary fistula has developed. Such was the case in 18 of the 25 war injuries reported by Robinson, the fistula developing within the first 10 days. Culp reported 6 cases, only one being recognized early. In Rusche's series of 5 cases, all were recognized late, ranging from 10 days to 10 weeks following injury. In one of these a fistula was not present and the first sign was a mass in the loin with sepsis. In late cases thorough investigation, including excretory urography and retrograde studies, should be carried out to determine the type and location of the injury and the condition of the kidney before deciding upon the necessary corrective measures. The longer the interval between injury and recognition or application of therapy, the more likelihood of the necessity for nephrectomy. Thus early diagnosis is essential. Every effort should be made to preserve renal function, particularly since the combat soldier comprises a young-age group.

CIVILIAN INJURIES

In civilian practice, the most common cause of injury to the ureter is surgical accident, most frequently sustained during surgery in the female pelvis. The age group here is relatively young also, emphasizing again the importance of conservation of the kidney. In a review of 36 cases of injury to the ureter collected from the Barnes Hospital and private practice, over 90 per cent were under 50 years of age, 16 or 44 per cent being in their thirties. In 35 of the cases, injury was due to surgical trauma and in one instance a ureterovaginal fistula developed 3 months after the application of radium for carcinoma of the cervix.

Surgical injuries to the ureter may be unilateral or bilateral and may occur by: 1) ligation, 2) crushing with forceps, 3) distortion from closely approximated sutures, 4) incision or partial division, 5) complete division, 6) resection of a portion of the ureter. Extensive stripping of the intact ureter is probably rarely complicated by any serious effects, as the anastomotic circulation of the ureter protects it from anemic necrosis.

The injury is rarely recognized at the time of the original operation. Such was the case in only one instance in this series. If the injury is discovered, the measures which may be applied will depend on the type and extent of the injury and the patient's ability to withstand prolonged surgery. In the event the ureter has been ligated, deligation and the insertion of a ureteral catheter would appear satisfactory. In the one case referred to previously, I was called in during an abdominal hysterectomy because the posterior wall of the bladder had been opened in separating it from the cervical canal. The trigone was exposed and the ureteral

although changes indicative of anatomic regression of ureteropelvic ectasis are not necessarily significant. Yet in relieving the obstruction we are primarily striving for the preservation of the kidney, the rehabilitation of renal function, and control or, better, eradication of existing infection. To our thinking the ravages of vesico-ureteral reflux are less than those of the grave pre-existing obstruction. I regret that time prohibits the demonstration of illustrative preoperative and postoperative urograms.

DR JOHN A. BENJAMIN (Rochester, N. Y.) I would like to compliment both Drs. Oimond and Osborne on their investigation, and I would like to show you some of our results at the University of Rochester.

(Slide) This first slide is from a girl about 4 years of age, we found some bands of tissue at the ureteropelvic juncture, which were removed, and a modified Schwytzer-Foley ureteroplasty was performed. This is 8 years later.

(Slide) This next case is that of a girl about 4½ years old.

First I would like to emphasize our indebtedness to Dr. Moore for guiding us as to the value of serial pyelography.

As I said, this is a girl about 4½ years of age. You will notice there are possibly three sites of obstruction. Whether they are true or functional, we have to find out.

These are 30 seconds apart. You will notice as we go on that this disappears—these two above persist.

(Slide) And you will see this ends rather nicely in the lower ureter, and that, I think, is due to some peristaltic waves. These two obstructions persist.

We resected 4 cm. of ureter, and this part, [indicating] when it was studied microscopically, showed very thin wall, with a great deal of fibrosis and very little musculature. We then carried out an anastomosis according to the procedure recommended by Dr. Boveé in 1897, which is a simple oblique anastomosis.

(Slide) This shows the postoperative result. I think you can see—after making anastomosis of the ureter to the pelvis—there is no obstruction below. This was not even explored, because we felt that serial pyelography certainly guided us to the fact that there was no mechanical or anatomic obstruction.

(Slide) That is a child of 3½ months. Our main trouble, of course, was this upper part here. In one stage we carried out a heminephrectomy and a ureterectomy, and this left the ureter to the lower pelvis about twice too long. The point came up: Where should we resect a ureter that is twice too long? We thought we would try anastomoses about midway, so we did.

Most of these pyelograms were done about 15 to 17 days postoperatively. We purposely leave a catheter down so we can obtain these pyelograms.

(Slide) This is a child 1 month old, with an ectopic ureteral orifice emptying into the urethra. The ureter was pulled through according to the method of Dr. Campbell, and then we carried out mucosa-to-mucosa anastomosis, making it a oblique or long as possible. Since then we have carried out cystograms—and there is no reflux. This is 19 months after this was done.

(Slide) This is a little girl with a reflux on one side. We pulled through the ureter according to the method described by Dr. Campbell. We have sub-

the ureter are found in the lower third. In 15 of the cases reviewed, or 75 per cent of the 20 cases in which the level of injury had been determined, the injury was within 6 cm. of the bladder.

Successful uretero-ureteral anastomosis depends on 1) careful approximation without tension, 2) preservation of the blood supply of the ureter, 3) adequate splinting and 4) control of infection. Avoiding tension on the suture line is extremely important, and the union should be water-tight. A sufficient number of sutures of fine chromic catgut should be used to accomplish the latter, but no more than is necessary. Leakage of urine at the site of anastomosis increases cicatricial tissue and the possibility of late stricture formation. Stripping the loose adventitia from around the ureter should be avoided. It is better if the cut ends of the ureter bleed. Polyethylene tubing seems preferable to the ureteral catheter for use as a splint.

Much has been said about the necessity for repeated dilatation following ureteral anastomosis and many urologists perform it as an accepted routine. Although I adhere to the principle, I have often wondered whether or not repeated dilatations of the ureter following a well performed anastomosis were really necessary or actually advisable. In some instances it seems logical to assume that the dilatation may add trauma and give rise to increased fibrosis. If the anastomosis is carefully and accurately performed without tension, the ureter properly splinted and infection controlled, one may rightfully wonder whether the repeated passage of a large caliber ureteral catheter is the deciding factor in a satisfactory end result. Also, if repeated dilatations are necessary in order to keep the ureter open, the anastomosis can hardly be considered as successful, and in such cases progressive hydronephrotic atrophy of the kidney with eventual nephrectomy is the likely course.

I would like to report an early result in a complicated case in which an end-to-end anastomosis of the ureter was performed in a low ureteral injury.

H. G., a woman aged 34, was first seen October 1, 1950. Two weeks before, an abdominal hysterectomy had been performed and on the fourth postoperative day she developed severe right renal pain. Excretory urograms revealed dilatation of the right renal pelvis and ureter. On the sixth day, the patient was cystoscoped and two catheters, Nos. 4 and 5, were passed easily up the right ureter with some relief of pain. The abdomen became increasingly distended, however, and on the tenth postoperative day the abdominal wound was reopened and 1000 cc. urine were evacuated. The ureteral catheters were found to be coiled up in the abdominal cavity. The abdominal wound was closed around a Pezzer catheter. When she was admitted to the Barnes Hospital 4 days later, the abdominal tube was in place and draining well, the bladder urine was purulent but her general condition was fairly good. Two days later she developed leakage of urine into the vagina through the cervical stump and the abdominal tube ceased to drain and was removed. Excretory urograms revealed a functioning right kidney with only moderate dilatation (fig. 1, A). On cystoscopy, a ureteral catheter blocked it 6 cm. up the right ureter but dripped purulent urine (fig. 1, B). Culture revealed coliform bacilli and B. proteumneous. Because of the gross infection, a nephrostomy was performed to protect the kidney until such time as the field

So, there was a boy who had received no treatment, who nevertheless went along for many years in apparent perfect health, though the condition was still progressing. He died from renal insufficiency and the kidneys showed absolutely no functioning tissue.

The operations we used in the 2 cases which we described were partly based on recent work on megacolon. You know it has been found that the lesion in Hirschsprung's disease is a congenital absence of the intrinsic nervous plexus in the terminal inch or so of the sigmoid, and that excision of this small segment of bowel corrects the condition.

In these 2 cases we tried the effect of excising the lower ends of the ureters, narrowing the ureters by removing a ribbon of tissue so that they fitted around a small rubber catheter, and then carrying out a procedure somewhat like that described by Dr. Campbell, drawing it down in the bladder through its normal course, through the vesical wall. However, we fear the results will not be good.

L B, a white woman, aged 32, was first seen March 30, 1938 because of a ureterovaginal fistula of 10 months' duration, which followed a hysterectomy. It was possible to catheterize the ureter through the vaginal fistula and retrograde studies revealed a functioning kidney with only moderate hydronephrosis (fig 2). Operation was performed on April 5, 1938, the ureter was exposed extraperitoneally, followed down to its entrance into the vagina, and was found to be free of any connection to the bladder. The bladder was opened, a small sound passed through the left ureteral orifice and forced through the stricture at 2 cm. The proximal end of the ureter was severed from its attachment to the vagina, a forceps passed through the intramural ureter from the bladder side and the lower end of the proximal ureter was grasped and drawn into the bladder. The

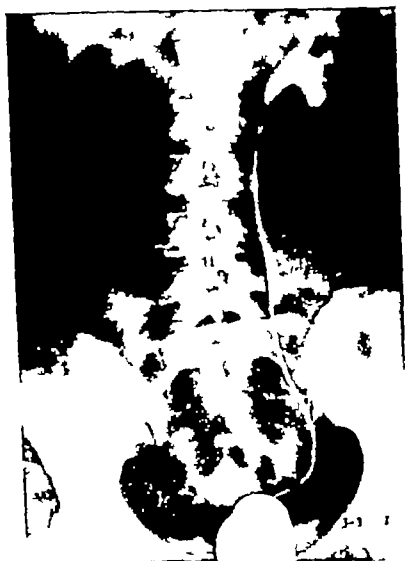


FIG 2 Preoperative retrograde left ureteropyelogram. Ureter catheterized through vaginal fistula. Mild hydronephrosis.

end of the ureter was split for about 1 cm, the flaps folded back and one suture of chromic catgut was taken through each flap and carried through to the posterior surface of the bladder (fig 3). A No. 8 ureteral catheter was used as a splint and brought out through the urethra. The bladder was drained by a urethral catheter passed alongside the ureteral catheter. The bladder was closed without suprapubic drainage. The ureteral catheter was removed on the twelfth postoperative day and the urethral catheter on the seventeenth day. Six weeks after operation a cystogram showed no evidence of regurgitation of bladder contents up the ureter (fig 4, A). Six months later cystoscopy showed an essentially normal ureteral orifice which admitted two No. 5 catheters without difficulty, and ureteropyelogram showed an essentially normal pelvis and ureter. A follow up in 1946, eight and one-half years later, shows a normal pelvis and ureter (fig 4, B) and she had had only one episode of mild urinary tract infection during the interval.

This method reproduces the normal anatomical relation of ureter to bladder

week before and after operation, and received penicillin and streptomycin for 5 days postoperatively.

Among various studies carried out on these animals we found that it was possible to visualize the anastomoses by sigmoidoscopic examination using a McCarthy panendoscope. It was seen that the tip of the ureter which had been pulled into the bowel varied widely in appearance. Instead of promptly sloughing off, in many it became swollen to form a firm, rounded nodule varying from $\frac{1}{2}$ to $1\frac{1}{2}$ cm. in diameter. In some instances this was red and markedly inflamed, in others it was gray with a rough, necrotic surface (fig. 2, A). In 7 dogs which were sacrificed at from 4 to 6 months one half of the anastomoses still presented such nodules. Histological sections through the nodules and anastomoses showed an extensive acute and chronic inflammatory reaction in the ureteral tip and the surrounding tissues (fig. 2, B). Although these were partially epithelialized, partly with intestinal mucosa and partly with ureteral mucosa, in none was the nodule completely covered.

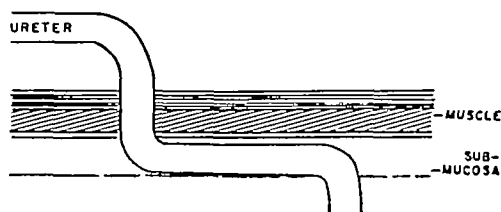


FIG. 1. Diagram of combination of Coffey 1 and Nesbit, Cordonnier procedures.

All of the dogs at autopsy were carefully examined for any evidence of obstruction of the ureter. In no instance did we find a kink or bend as the cause of obstruction, the lower ureter appearing in most instances surprisingly free and redundant. Obstruction, when present, was found to be just at the mucosal junction. By perfusing the ureters at autopsy with saline we found that where dilatation of the ureters existed it extended down exactly to the mucosal junction where there was stenosis. Examining such specimens from the mucosal side the dilated distal portion of the ureter could be seen through the entire length of the submucosal trough down to a small opening at the junction of ureteral and sigmoidal mucosa. From these findings we concluded that the ureteral tip within the lumen of the sigmoid acted as a point of entrance for infection, and as the tip often did not slough completely for a period of at least many weeks, it remained as a site of acute and chronic inflammatory reaction in immediate proximity to the actual anastomosis. The scarring which results could well account for the fact that obstruction when present appeared at the mucosal junction.

We carried out a series of anastomoses making end to side anastomoses of the Nesbit or Cordonnier type between the mucosa of the ureter and bowel. We used either one or two layers of sutures, interrupted or continuous, and included the full thickness of bowel in some and just the mucosa in others. The great differences in size and anatomy between man and dog make any precise comparison of operative details of little value. Of 21 dogs operated on in this manner 14 died within the first week from generalized peritonitis as a result of leakage at the suture line. In no instance was there retraction of the ureter. This leakage

persisted for 4 months and then cleared permanently, and he began gaining weight and energy. When last seen 8 years later he was a tall, strong boy on his school cross-country team, and had never had any further urinary trouble. Excretory urography showed a functioning kidney, but persistent hydronephrosis of about the same grade as previous to operation (fig 1 B).

Here there was relief of symptoms, prevention of infection and halting of renal deterioration.

Case 2 Henry Ford Hospital No. 379169, a 9-year old boy gave a 2 year history of recurrent abdominal pain, nausea and vomiting and no urinary symptoms. Excretory urography showed delay in the appearance of the medium and marked dilatation of the calyces on the left, and some pyelectasis on the right,



FIG 1

but normal calyces (fig 2 A). At operation a stricture of the left ureteropelvic junction was treated by using a Foley plastic with temporary nephrostomy and ureteral splint. The abdominal pain disappeared, but a urinary infection persisted for 4 months until cleared by penicillin. After this he felt well and became active in athletics. Excretory urography recently 5 years after operation, shows persistent hydronephrosis on the left but no progression. There possibly may be a little advance in the pyelectasis on the other side (fig 2, B).

Here there was relief of symptoms and halting of the progress of the hydronephrosis. The other kidney will bear watching.

Case 3 Henry Ford Hospital No. 470353, a 2½ year old girl had been followed for 1½ years because of recurring febrile attacks accompanied by pyuria and pain on urination. Cystoscopy showed pus cells from the left kidney and reduction of function on the left as compared to the right. Pyelograms showed moderate hydronephrosis with obstruction at the ureteropelvic junction on the left and slight similar obstruction on the right but with no pyelectasis. At operation an

of flow was found in general to correlate well with the degree of ureteral dilatation and hydronephrosis. Figure 3, *B* shows typical recordings obtained following a direct anastomosis which functioned satisfactorily. In several instances,

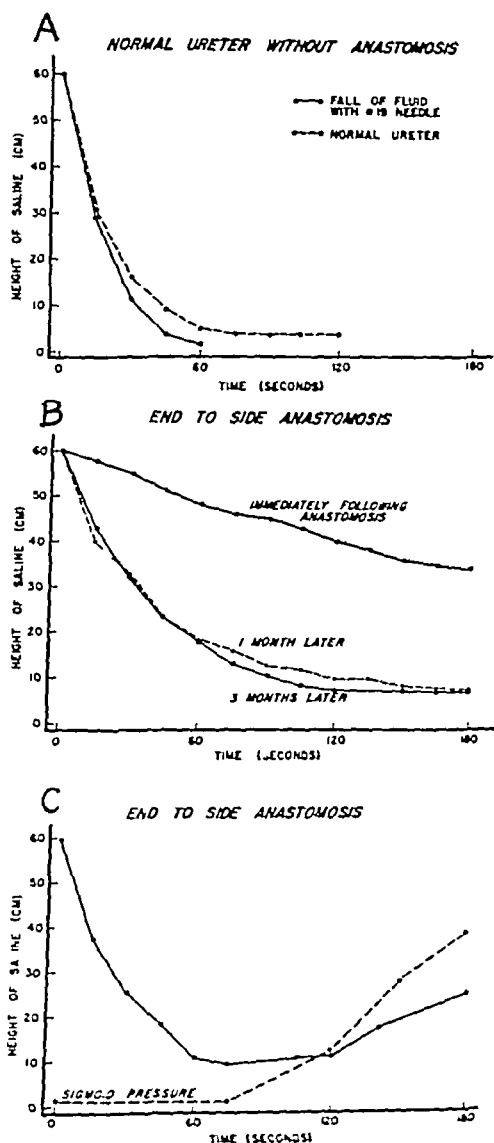


FIG. 3. *A* graph of flow through a normal ureter without anastomosis. *B* graph of flow through end to side (Nesbit-Cordonnier) type anastomosis. *C* graph showing ureteral flow followed by reflux into ureteral cannula when sigmoid pressure was raised.

however, severe pyelonephritis was found to be present despite adequate flow rates and seemingly adequately functioning anastomoses.

To determine why pyelonephritis occurred in such cases we re-explored several animals to test them for reflux. At operation the ureter was cannulated and the flow determined. The sigmoid was then clamped with a rubber band into tight clump well above the anastomosis and fluid was introduced through a rectal tube

There has been apparent improvement but we know that children with damaged kidneys, even when the damage is progressive may live for years in apparently good health

Case 5 Henry Ford Hospital No 624064, a 7½ year old boy for 2 years had had recurring bouts of fever, nausea and vomiting, left upper quadrant pain, progressive nervousness, and enuresis Cystoscopic examination showed clear urine from the right ureter and marked pyuria on the left Pyelogram showed bilateral ureteropelvic obstruction with mild pyelectasis on the right and moderately advanced hydronephrosis on the left

A Foley plastic operation was done on the left ureteropelvic juncture, using splinting catheter and nephrostomy drainage When last seen 5 months after operation, he had had no attacks similar to those he had previous to operation, was having no urinary symptoms had gained 20 pounds, and his urine was clear



FIG 3

An excretory urogram made 4 months after operation showed no shadow on the left side

Operation gave symptomatic relief, and cleared the infection but it is questionable if there is any restoration of function It is advisable to observe the other kidney from time to time to determine whether the pelvic dilatation on the other side should be treated

Case 6 Henry Ford Hospital No 476220, a 10 year old boy was admitted because of persistent low grade fever, easy fatigue and slow weight gain He had had recurring peri-umbilical and left flank pain for 3 years, with a diagnosis of mild left hydronephrosis due to ureteropelvic obstruction His urine was usually clear He was a poorly nourished boy who appeared chronically ill and after a period of general investigation intravenous and retrograde pyelograms were made which corroborated the diagnosis of mild left hydronephrosis (fig 3-4)

A Foley plastic operation was done with a splinting catheter and a nephros-

sure. It was found that when the pressure within the sigmoid reached from 10 to 15 cm. of water, flow through the ureter ceased. If the pressure was reduced ureteral flow was promptly resumed. Thus the submucosal trough worked effectively as a valve so far as fluid descending the ureter was concerned. The segment of ureter lying beneath the muscular layers of the bowel could evidently be compressed by increased pressure within the bowel lumen.

In the next group of 15 dogs we constructed a submucosal trough again similar to the Coffey I and then made an end to side anastomosis of the ureteral mucosa to the sigmoid mucosa near the distal end of the trough. This was done with interrupted 4-0 chromic catgut sutures through the entire ureteral wall and the mucosa of the sigmoid. These cases were entirely similar to the Coffey I anastomoses except that the tip of the ureter was anastomosed to the bowel mucosa instead of being pulled into the sigmoidal lumen. Twenty-one such anastomoses were done. Sixteen of these anastomoses were tested for reflux at a secondary

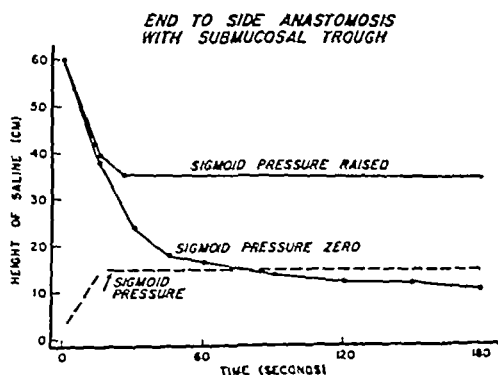


FIG 5 Flow through end to side anastomosis with submucosal trough (combined type) with sigmoid pressure zero, and sigmoid pressure raised

operation and in no instance was any backflow noted, the ureteral flow merely ceasing (fig 5). Pyelonephritis was present in 6 kidneys although in 3 it was very mild in amount. Of 16 anastomoses which were tested for the rate of flow of fluid through the anastomoses, in 14 instances it was good or excellent. In only one instance did leakage occur at the suture line, and the ureter in this case had been cut very much more obliquely than the others, in an attempt to determine the upper limit to which this could be done. The anastomoses when viewed through the sigmoidoscope, or at autopsy, showed no exposed nodule or tip as in the Coffey type dogs.

Five dogs had stab type anastomoses performed in which the ureter was pulled through a stab wound in the sigmoid and fastened in place. Two of the dogs died promptly of peritonitis from leakage about the anastomosis. One was found to have marked reflux.

DISCUSSION

Several points seemed to stand out from these studies. In the Coffey I operation the tip of the ureter within the sigmoid did not, in many instances, slough off promptly to provide an accurate anastomosis of the ureteral and sigmoidal mucosa. Instead it often persisted for a period of at least several months and

ureterocele was excised flush with the bladder floor, the mucous membrane of the cut edges being approximated with interrupted catgut sutures

During the 3 years after operation she had repeated febrile episodes with pyuria and dysuria which yielded promptly to sulfadiazine. The incidence diminished in frequency with the passage of time. Two years postoperative she had fair concentration of indigo carmine excretion and moderate hydronephrosis and hydro-ureter on the right, the obstruction being apparently at the bladder end of the ureter. When last seen her urine was negative and she was a healthy appearing, well nourished child.

Gross and Clotworthy have stated that ureteroceles should not be excised, but only incised. Their reasoning is sound but in a large ureterocele as this which partly extrudes through the urethra, excision seems advisable. This patient will have to be followed carefully because of the dilatation of the right pelvis.

Case 10 Henry Ford Hospital No. 460651, a well nourished 8 year old boy had had pyuria for a year. An excretory urogram showed a nonfunctioning right kidney and a left hydronephrosis. An olive-sized right ureterocele was found to be acting as a valve to the urethra and pressing on the left ureteral orifice causing obstruction. After excising the ureterocele a finger could be passed up the markedly dilated lower ureter. Convalescence from operation was uneventful. He disappeared from our observation and when seen 5 years postoperative he was found to be a well grown, healthy looking boy. His residual urine was 500 cc and his phenolsulfonphthalein output was 33 per cent in 1 hour. A cystogram showed a voluminous bladder with reflux up the right ureter. A left hydronephrosis and a nonfunctioning right kidney were again revealed by excretory urography. Endoscopy revealed some loose tissue on each side of the posterior urethra which might be valves. The patient undoubtedly should have further treatment, probably starting with a long term cystostomy and right nephro-ureterectomy.

It is unfortunate that this boy was not seen earlier before the ureterocele had caused such extensive damage to the right ureter and kidney.

Case 11 Henry Ford Hospital No. 583114, a 2 year old girl had anemia, recurring fever, pain with urination and pyuria for a year's duration. Pyelograms showed marked hydronephrosis and hydro-ureter on the right and the same, to some less degree, on the left. The nonprotein nitrogen was elevated to 49 mg per cent and the phenolsulfonphthalein output not over 20 per cent in 1 hour. The tortuous ureters were straightened by excising their upper portion and symptoms improved for a year, after which they recurred. A cystogram showed bilateral reflux into the ureters (fig 4, 1) and she was then subjected to operation at the lower end of the ureters. The ureters were decreased in caliber by removing ribbons of tissue from their lower half or two thirds and reforming them over small rubber catheters. The intramural portion of the ureters was dissected and the ureter drawn into the bladder until the lower end could be excised up to the beginning of the narrowed portion. We hoped thus to restore the valve-like action of the ureteral orifice. Three months after operation, however, a cystogram showed marked bilateral reflux and increased deterioration of the kidneys (fig 4 B).

Case 12 Henry Ford Hospital No. 611633, a 2 year old girl had recurring fe-

EVALUATION OF COMMON METHODS OF URETERO-INTESTINAL ANASTOMOSIS: AN EXPERIMENTAL STUDY

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While uretero-intestinal anastomosis has lacked widespread popularity among surgeons because of difficulties which may be inherent in the procedure, it has not lacked advocates who ever seek the perfect method. The history of the operation has revolved about three hazards: peritonitis, ascending infection, and obstruction to the upper urinary tract. To these there has recently been added a fourth: reflux to the kidney.

Peritonitis was the first complication to be conquered when the submucosal principle was applied by Coffey in 1913. Leakage at the site of anastomosis was virtually eliminated and peritonitis ceased to be the foremost menace. Yet for the ensuing 25 years, ascending infection and obstruction continued to exact a high mortality and devastating morbidity. Although the dramatic improvement stemming from the introduction of modern antibacterial agents gave good cause for encouragement, up until three years ago a satisfactory operative technique had not been found which did not incorporate the submucosal tunnel.

Then Cordonnier and Nesbit, working independently, gave the first extensive clinical trial to direct anastomosis of mucosa of ureter to mucosa of bowel. The adoption of this technique enjoyed a generous reception by urologists because it seemed to decrease the incidence of urinary obstruction. However, with added experience, it became evident that although possibly superior to the Coffey technique, it was not the final solution to the problem. In abandoning the submucosal principle the complication once satisfactorily eliminated apparently returned—peritonitis due to leakage. Furthermore, reflux arose as a frequent complication.

We have carried out an experimental study in an effort to evaluate the merits of the basic surgical principles employed in these operations. Only animals can provide conditions controlled adequately to allow statistical analysis of necropsy findings at various periods after operation. The influence of the following factors was evaluated: a) the submucosal tunnel, b) implantation of an intraluminal segment of ureter and c) a mucosa-to-mucosa union. This was done by utilizing four techniques (fig. 1).

1) The Coffey technique, incorporating a submucosal tunnel with an intraluminal segment of ureter (fig. 2, A).

2) The Cordonnier technique, exemplifying the mucosa-to-mucosa anastomosis (fig. 2, B).

3) Direct implantation with a redundant intraluminal segment of ureter (fig. 3, A).

Read at annual meeting, American Urological Association, Chicago, Ill., May 1-3, 1951.
We express appreciation to Albert H. Bowker and Stephen G. Allen, Jr., Department of Statistics, Stanford University, for aid in statistical evaluation of the results of this study.

lateral reflux and apparent reformation of the hydro-ureters (fig 5, B) Symptomatically the child seems improved but we are much disheartened by the last examination and fear the improvement is only temporary

These last 2 cases, if our diagnoses are correct, represent different stages in the condition known as megaloureter. The underlying cause of this condition is in dispute, but its usual course consists of progressive dilatation of the ureters and pelvis, reflux and infection ending in death from renal insufficiency after varying lengths of time. One boy afflicted with this condition, and who received no surgical treatment, whose course we knew about from the age of six, lived in apparently vigorous health until his death from renal insufficiency at the age of eighteen.

It is, therefore, difficult to appraise the effect of treatment. In case 11 we can be sure the treatment was ineffective. Only the passage of years can tell whether in case 12 the treatment availed anything.

Certainly, as we review these 5 cases of plastic surgery at the lower end of the ureter, we can take little satisfaction in the results. In only 1 case (case 9) has a cure been obtained. The other patients have showed only temporary improvement. This is in contrast to the results of plastic surgery at the upper end of the ureter.

SUMMARY

We have here reported on 7 cases of plastic operation at the upper end of the ureter and on 5 cases of plastic operation at the lower end of the ureter, all in children.

The results of operation at the upper end of the ureter are uniformly good, in great contrast to the results at the lower end.

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The presence of reflux was determined at the time the India ink mixture was injected into the isolated segment of bowel. If present, it occurred at a pressure of approximately 10 cm of water.

Leakage was considered to have occurred if general or localized peritonitis was present.

The site, cause and degree of obstruction were determined on the basis of three observations: gross inspection of ureter and kidney (fig 4, 1), study of post

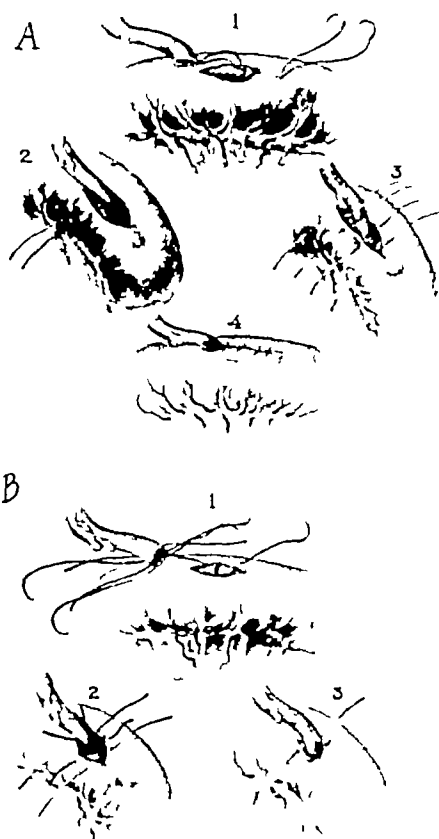


FIG. 2. A, Coffey 1-1. Plating, anchor suture, 2, end of ureter drawn into bowel, 3 and 4, closing muscularis over tunnel.

B, Cordonnier 1. Plating mucosa to mucosa sutures, 2, sutures tied, 3, closing muscularis around ureter, fixation sutures to adventitia.

mortem retrograde pyelograms (fig 4, B), and examination of the anastomosis site in the cleared preparations (fig 5). Obstruction was recorded as being absent if there was no hydro-ureter or hydronephrosis. If the ureter was hugely dilated and there was marked hydronephrosis with atrophy of the renal parenchyma, obstruction was graded as severe. Intermediate degrees were classified as mild or moderate by comparison with others in the entire series.

A similar system of grading was used to indicate infection of the upper part of the urinary tract. Infection was considered to be absent if ureteral urine obtained

transurethraly incised upward with miniature cystoscopic scissors, the incision being carried into the bladder for about 2.5 cm. Thus the urine came to drain into the bladder instead of into the urethra and the incontinence was cured. I have successfully done this in four other similar cases of ureteral ectopia, sparing the patient the ordeal of ureteroneocystostomy.

In a somewhat unusual case, a 3 year-old girl with incomplete left ureteral reduplication, the ureteral branch to the lower pelvic segment was strictured at its junction with the branch to the upper pelvis, the bifurcation occurring at about midureter. In this case the stricture was incised longitudinally with extension of the opening upward in the dilated ureteral branch for 1.5 cm. and equally downward in the normal single ureter, below the point of bifurcation. A 10F T-tube was left indwelling for 2 weeks, one arm extending upward in the dilated branch to the lower pelvis, the other downward in the normal ureter. Gratifying relief of the obstruction was achieved.

In some instances of ureteropelvic junction obstruction complicated by tortuosity and kinking of the adjacent ureter, excision of this area with a generous segment of the renal pelvis followed by oblique ureteropelvic anastomosis has been most successful.

In closing I would like to suggest the use of a simple method for the transvesical treatment of ureterovesical junction strictures with dilated redundant ureter above. I have been using this procedure for about ten years and, although it probably bears no novelty, I have not found it described in the literature. For convenience we have designated it as the ureteral pull-through or sleeve excision operation, the various steps of which are indicated on the screen. In brief, the stenosed ureteral orifice and adjacent stricture are elevated by a hooked probe and incised upward for 2 to 3 cm. which lays open the lower end of the ureter and often means opening into the perivesical space as well. Yet this is of no moment because cystostomy drainage is employed postoperative for 2 to 3 weeks.

The exposed ureter is grasped with hemostats at four equidistant points and by a circular incision is mobilized from its adjacent bladder muscle. Using the knife handle for blunt dissection and exerting traction on the ureter, the duct is mobilized and pulled through, in some cases of pronounced ureteral redundancy with angulation and kinking, for as much as 5 or 6 inches. The excess ureter is then excised, the proximal end of the duct being sutured mucosa to mucosa to the adjacent incised bladder wall. A four-eye catheter of diameter as large as the ureter will comfortably accommodate is introduced upward to the kidney pelvis and brought out with the bladder drainage tube through the suprapubic opening. This ureteral tube is left indwelling 2 to 3 weeks. By this relatively simple procedure not only can considerable excess or redundant ureter be readily removed, but a new and widely patent orifice established. In one case, a 13 month old boy, excision of the entire ureteral redundancy was prohibited by sclerotic peri-ureteral fibrotic fixation at a point just below the level of the iliac crest is later disclosed by long exposure.

In the cases in which obstruction has been relieved, some show vesico ureteral reflux while others do not, and renal functional improvement has been achieved.

at necropsy contained no pus cells or bacteria and there was no gross or microscopic evidence of pyelonephritis or ureteritis. Mild pyelonephritis was manifested by pus cells and bacteria in the ureteral urine and minimal inflammatory reaction in the ureter, renal pelvis and parenchyma. If the condition was classified as moderate pyelonephritis, the urine was grossly purulent, and the microscopic examination of the kidneys showed dense infiltration of the medulla with leukocytes, subcapsular collections of inflammatory cells and small cortical abscesses. Severe pyelonephritis was evidenced by abscesses of the parenchyma, a thickened renal capsule, and scar tissue in the cortex and medulla. Ureteritis was usually quite marked. Perinephric abscesses were included in this group.

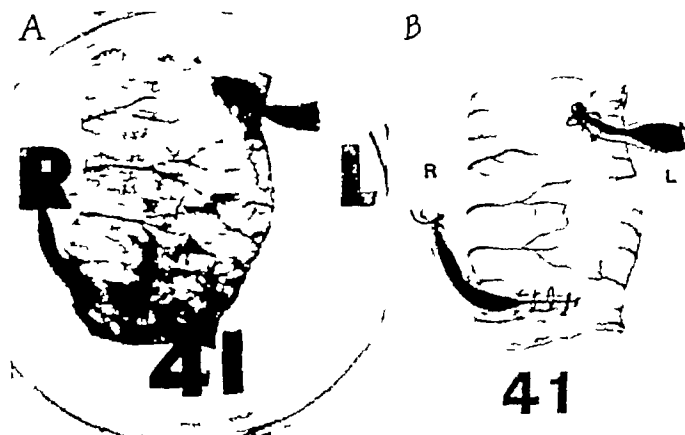


FIG 5 Cleared specimen, dog No 41. A, photograph, B, diagram. Right Colectomy, left, direct. Dog died 45 days postoperatively. Constriction of tunnel on right produced mild hydro ureter and mild hydronephrosis. Stenosis of intraluminal segment on left produced moderate hydronephrosis.

The various complications were tabulated and subjected to statistical analysis by the chi square test of homogeneity for contingency tables. Contingency tables are formed by listing the number of complications observed for each operative technique, as in the following example concerning reflux.

TYPE OF OPERATION	NUMBER OF CASES OF REFLEX		Total
	With Reflux	No Reflux	
Direct	2	18	20
Cordonnier	7	12	19
Colectomy	0	21	21
Combined	0	20	20

Clearly, these frequencies differ between themselves, but our interest is to determine whether the differences arise by chance, or whether it may be assumed that the observed differences are inherent in the different operative technique. To make the decision the hypothesis is set up that all types of operation are homogeneous with respect to reflux. A chi-square statistic is calculated from the data

quently done cystograms, and there is no reflux period. You can see here that the twisted ureter is straightened.

DR JOHN K. ORMOND (Detroit, Mich.) We did not report any operations on midureter because we had not seen any cases of that kind. We realize that this is a very small series of cases.

Our reason for giving this paper is that it contains the total product of over 20 years of a fairly active pediatric service. We reported here only 2 cases of ureterocele, and Meredith Campbell tells me he has seen 94, that's quite a difference.

There are a few points I would like to enlarge upon in connection with this paper. First, I show a slide giving the indications for urological investigation in children, and want to call particularly to your attention No. 8, that is, failure of weight gain or growth in an infant who is on a good feeding program. We think that is a very definite indication.

Next I wish to discuss the operations on the upper end of the ureter. There seems to be no theoretical reason why these operations should not be as applicable to children as to adults, and I think our results speak for themselves. It is interesting, and may have some significance, that in our group, six of the 7 patients were boys, and in all cases the chief lesion was on the left side.

The rest of my remarks are concerned with the condition represented by the last two cases, that is, megalo-ureter.

The underlying cause of this condition is not known, it must be some neuromuscular disturbance involving the bladder and the ureters in whole or in part. There is considerable confusion in the literature as to what should be designated megalo-ureter. I am inclined to believe it should only include cases in which the condition is bilateral, appears early in life, and in which no sign of any organic obstruction can be found. Its usual course consists of progressive dilatation of the ureters and pelvis, with reflux and infection, ending in death because of renal insufficiency. So far as I know, no cure has been obtained in any cases, and the pitfalls in the way of estimating whether even minor benefit has been obtained from any method of treatment are illustrated by the following patient, who received no operative treatment.

(Slide) This was an active boy of 6 years, who came to us because of pyuria. The cystogram showed marked reflux, hydro-ureter and hydronephrosis. The problem was thoroughly discussed with the parents, and we had further discussions with other urologists, and the patient's parents finally decided to do nothing, but let nature take its course.

That boy went up through school and high school. He was an intellectual, athletic and social leader. He grew well. He went to college and continued his course as a leader among his fellows. One day in college he had a little difficulty in moving his left hand and got on a train and went home immediately, and died 2 days later in coma.

(Slide) These are the results of the autopsy, which show that there had been definite progress, but not tremendous progress, since the time he was seen at 6 years of age.

(Slide) This shows that the bladder was comparatively normal. It was a little thickened but showing no evidence of obstruction at the ureterovesical junction.

from the direct course of the ureter through the intestinal wall. Whatever non pathological barrier against reflux there is, is provided by the submucosal course. The action is apparently that of a valve, as suggested by Coffey.

The low incidence of reflux after the direct method would apparently be higher were it not for a pathological barrier—stricture formation in the intraluminal segment. In a previous study of the end of the implanted ureter, we found that

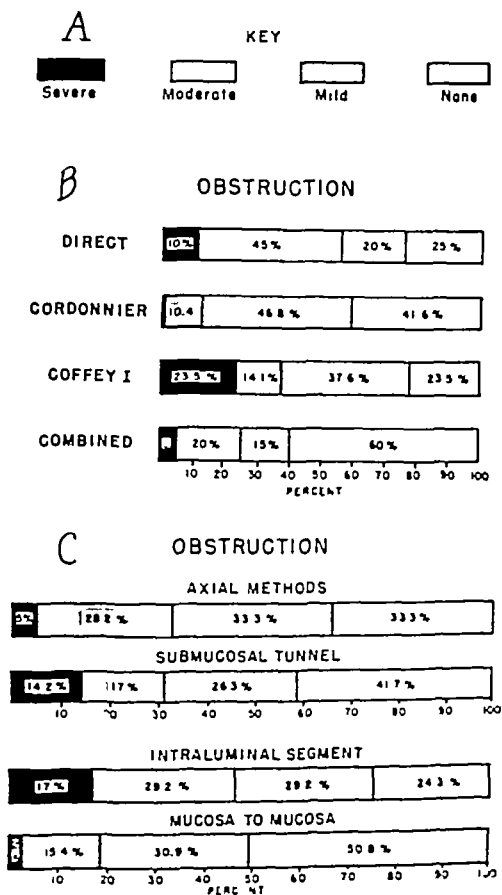


FIG. 7-1. designations for various degrees of obstruction and infection

B, obstruction following various operations

C, incidence of obstruction in grouping techniques with a common principle. Axial methods, direct, Cordonnier, Submucosal tunnel, Coffey I, combined. Mucosa to mucosa, Cordonnier, combined.

after operation the intraluminal segment became the site of obstruction from early acute ureteritis followed by stricture formation.

As concerns leakage (fig. 6, B), there were two cases of generalized peritonitis, both followed the Cordonnier operation, in both the ureter sloughed from the anastomosis. Localized peritonitis, evidenced by a walled off abscess surrounding the anastomosis, was observed in two additional instances after the Cordonnier and in one instance after direct implantation. In applying the di-square principle

URETERO-ENTEROSTOMY EXPERIMENTAL STUDIES

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Uretero-enterostomy still remains an important limiting factor in the cure of infiltrating carcinoma of the bladder. When diversion of the urinary stream from the bladder can be done safely so that patients will be assured of good renal function over a period of years then, and only then, will radical surgery on the bladder be carried out at the optimum time. Despite the many types of uretero-enterostomy which have been advocated only a few general types have continued to be widely used. Prior to 1945, the Coffey¹ 1 type of anastomosis enjoyed the greatest popularity and was perhaps performed more than all other types of operation together. This procedure consisted essentially of a submucosal trough in the sigmoid and a pull through of the ureter at the distal end of this trough. The results from this operation were in general superior to the stab type anastomosis which consisted of a pull through of the ureter without the formation of any trough. In 1945, Nesbit² and Cordonnier,³ working independently, each described a direct anastomosis of the tip of the ureter to the wall of the sigmoid, with results so encouraging that it has since been used by many operators. The results from any of these procedures were, however, far from being uniformly successful. In 1950, Leadbetter⁴ described a combined form of operation in which a direct end to side anastomosis was made at the distal end of a Coffey 1 type trough with encouraging results (fig. 1).

In reviewing the literature concerning this important subject we were impressed by the paucity of experimental work which had been done to study the anastomoses of each of these types functionally and morphologically. We felt that a series of experimental anastomoses carried out on dogs, and studied in various ways, might give us information of value which would improve the clinical results.

We first performed 20 Coffey 1 type anastomoses on 16 dogs. In each case we transected the ureter close to the bladder and after cutting the tip obliquely placed a traction suture through its tip. An incision approximately 2½ cm. in length was then made down to the mucosa of the sigmoid and the lateral margins were dissected back quite widely leaving a roomy trough. Near the distal end of this incision a small opening was made in the sigmoid mucosa and the ureter was drawn through this opening into the bowel for approximately 1 cm. and held at that point by the traction suture. The margins of the trough were then approximated over the ureter with interrupted 5/0 silk sutures, care being taken not to hold the ureter snugly. The dogs were placed on a low residue diet for 1

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Read at annual meeting, American Urological Association, Chicago, Ill., May 22, 1951.

¹Coffey R. C. J. A. M. A. 56: 397-403, 1911.

²Nesbit R. M. J. Urol. 61: 725-734, 1949.

³Cordonnier J. J. Surg., Gynec. & Obst. 88: 441-446, 1949.

⁴Leadbetter W. I. J. Urol. 65: 818-830, 1951.

the tissue spaces in the wall of ureter and bowel. Stenosis of a mucosa to mucosa stoma is a much less frequent complication than is the obstruction caused by an intraluminal segment.

In comprising the most frequent complication noted, infection occurred without significant difference in all techniques (fig 10, 1). A comparison of the *indirect* methods with the submucosal tunnel procedures revealed no significant difference, nor did a comparison of the intraluminal segment with the mucosa to mucosa methods.

The high incidence of infection subsequent to all four operations is readily understandable if one looks upon upper urinary infection as a secondary complication dependent on obstruction or reflux. Either or both complicate all methods.

CAUSES OF OBSTRUCTION

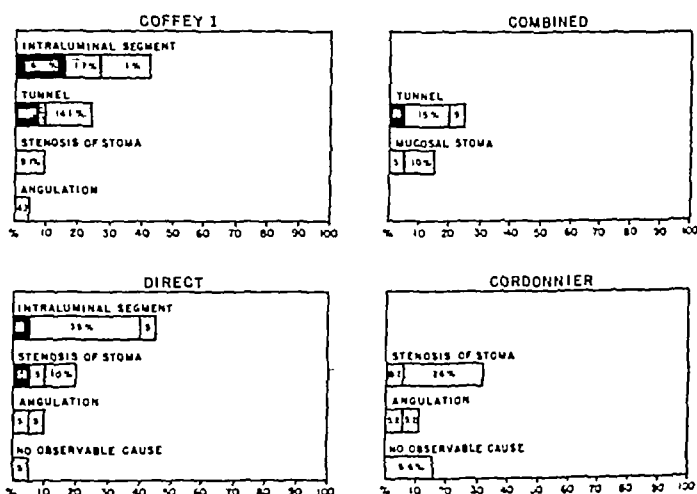


FIG 9

no method is significantly free of both. Complete absence of infection depends upon the elimination of both obstruction and reflux.

The most *severe* infection was observed in the groups undergoing the direct and Coffey 1, paralleling a high incidence of obstruction in these methods, while the lowest incidence of *severe* infection occurred after the Cordonnier. The same is true clinically: infection is most dangerous in the presence of obstruction. Although the Cordonnier with its susceptibility to reflux does not reduce the incidence of infection, the infection may be less severe.

Obviously, in addition to the broad surgical principles followed in performing any operation, the technical precision of their execution influences the results considerably. In uretero-intestinal anastomosis delicate handling of the ureter, use of fine suture material, precise union of ureter to bowel, and the avoidance of tension on tissues are important precautions which all contribute to proper healing. By preserving the tenuous ureteral blood supply and avoiding strangulation there is less likelihood of infection, ureteral obstruction and leakage.

One of the most significant conclusions to be drawn from these experiments

was discouraging and impressed us with the value of the submucosal trough which supported the Coffey anastomoses and helped prevent leakage. Of 15 anastomoses which were examined when the dogs were sacrificed at from 1 to 5 months post-operatively, pyelonephritis of considerable extent was found to be present in 10 instances.



FIG. 2. A: nodular ureteral tip 1 week following Coffey 1 operation contrasting with stoma of end to side anastomosis. B: section through ureteral tip nodule and stoma 9 weeks following Coffey 1 procedure showing acute and chronic inflammation in the nodule.

We tested the patency of the anastomoses by cannulating the ureters at a secondary operation and determining the rate of flow of saline through the intact anastomosis. These were done exactly like a venous pressure determination. A column of saline 60 cm. high was allowed to flow through a ureteral cannula and the height of this fluid charted at intervals up to 3 minutes. The flow was compared with that of a normal ureter without any anastomosis (fig. 3, 4). The rate

ureter might lend added security to the anastomosis. However, in our hand, this modification was inferior to the original operation. In an additional 7 dogs subjected to bilateral implantations by this method, leakage took place in 3 of 14 implants (21.4 per cent), generalized peritonitis occurred when the ureter sloughed from the anchor suture (fig. 11). Our opinion, therefore, is that until some superior modification of an axial implantation is worked out, the combined operation is the most desirable.

We are now endeavoring to improve the technical application of the underlying surgical principles of the combined procedure. In addition to the precautions previously mentioned, special attention is being given to the following steps:

1) The opening in the end of the ureter is made as large as possible by enlarging the ellipse with a proximal slit.

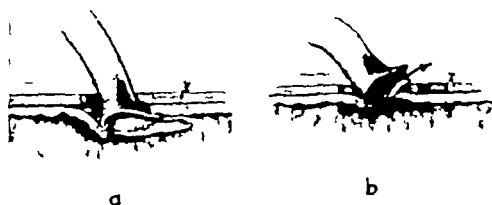


FIG. 11. A, modification of axial implantation using anchor suture. B, generalized peritonitis resulting from slough of ureter from anchor suture.

2) Care is exercised to make the opening in the mucosa of the bowel no larger than required to precisely accommodate the end of the ureter.

3) In forming the submucosal channel, a) the incision is carried well down to the mucosa, taking care to divide the fibrous tissue of the submucosa, b) the muscularis is dissected well back from the intramural course to be taken by the ureter, and c) in reconstructing the muscularis over the ureter the sutures are tied very loosely. These precautions are taken to assure an adequately large stoma, to prevent infection along the course of the ureter and to avoid constriction of the submucosal channel.

By meticulous attention to all these details and the use of adequate antibiotics we believe that the best results attainable will be secured by this method. A high percentage of per primam healing is assured, the danger of leakage and reflux is practically eliminated, and constriction of the lower ureter with subsequent obstructive changes and ascending infection is reduced to a minimum.

SUMMARY

In an attempt to evaluate the relative merits of the different surgical principles employed in modern methods of uretero-intestinal anastomosis, five variations have been tested in 47 dogs. By comparing the incidence of reflux, leakage, obstruction and infection following operations utilizing a submucosal tunnel, an intraluminal segment of ureter and a mucosa-to-mucosa union, it was found that the combination of a mucosa-to-mucosa union with a submucosal tunnel proved to be the most satisfactory method. The submucosal tunnel affords security

increasing the sigmoidal pressure while ureteral flow continued. We found that fluid flowed readily down through the anastomoses until the bowel pressure was raised, following which fluid actually backed up again into the ureter (fig 3, C). This showed the occurrence of reflux even at fairly low bowel pressures. Such reflux was found in 9 of 18 anastomoses tested in this manner. No reflux was found in the 7 anastomoses of the Coffey type which were tested.

At autopsy, excising the kidneys, ureters and sigmoid intact, it was possible to clamp both ends of the sigmoid segment and inject this with skiodan. In dogs which had had end to side anastomoses, prompt reflux to the kidneys was shown by x-ray in many instances (fig 4). The ease with which this reflux could occur



FIG 4. Skiodan injection of excised sigmoid segment showing unilateral reflux following end to side anastomosis. Note unilateral renal scarring.

was shown in some of these specimens when wave-like impulses could be seen ascending the ureter when the sigmoid was squeezed. If the pelvis of the kidney in such a specimen was opened quantities of fecal stained fluid would flow from the pyelotomy. The pyelograms obtained in this manner often appeared normal, but sections of the kidneys revealed that despite lack of hydronephrosis, pyelonephritis was frequently present. From those specimens in which reflux occurred so easily, it seemed that pyelonephritis was almost inevitable.

To determine whether the lack of reflux in the Coffey group was due to valve-like action of the submucosal trough, as Dr. Coffey believed, we carried out another experiment.

In 4 dogs we constructed submucosal troughs exactly similar to the Coffey type but the ureter, instead of being cut off and inserted in the bowel, was left in continuity with the bladder. Several weeks later we re-explored these animals. By cannulation of the ureter a free flow was proven to occur through the ureter into the bladder. Then, in our test for reflux, we increased the sigmoid pres-

DISCUSSION

DR JUSTIN J. CORDONNIER (St. Louis, Mo.) I wish to congratulate Dr. Woodruff, Cooper and Leadbetter, and Drs. Weyrauch and Young on their excellent and carefully analyzed experimental work in ureterosigmoid anastomosis. The fact that two groups, working completely independently, should arrive at almost identical conclusions adds considerably to the practical importance of their findings, and the modifications which they have evolved may prove of value in the technique for ureterosigmoid anastomosis.

There is one factor common to both which I believe should be given consideration in evaluating their results, namely, that all were obtained on dogs. All of us who have done experimental uretero-intestinal transplants in dogs are familiar with the many technical difficulties encountered. The ureters of the dog are quite small, making particularly difficult plastic procedures that require careful suturing. In addition, problems of bowel preparation present a definite hazard as regards immediate postoperative infection. The problem of urinary leakage, for instance, which seems to present a distinct hazard in the experimental animal, has not been present at the site of an anastomosis postoperatively in a single case in our clinical series. Therefore, I am not wholly convinced that the experimental findings which have been presented would necessarily apply in the human.

I am in complete accord with the finding of a cherry-like nodule within the lumen of the bowel at the site of the anastomosis in the Coffey I procedure, as described by the essayist. It was this very finding at autopsy following a Coffey I transplant which led me to do the first mucosa-to-mucosa anastomosis. The principal objection to the direct method offered by both groups was that of reflux. Therefore, I think it might be well to analyze our clinical results with this finding in mind.

In a recent analysis of 60 cases of uretero-intestinal anastomosis done by the mucosa to mucosa method, 26, or 40 per cent gave a history of urinary sepsis as manifested by chills and fever, and of these, 14 were minimal, consisting of two or less episodes of sepsis. In my opinion sepsis has not presented any great problem in our series.

An pyelograms have been present postoperatively in only 5 kidneys in our series of 64 cases. With one exception, these were present in kidneys which were nonfunctioning preoperatively.

We have studied 16 patients for reflux by filling the colon with a skiodine enema under considerable pressure. One of these patients had a preliminary nephrectomy so there were 31 kidneys studied. Five ureters, or 16 per cent showed reflux, a considerably lower percentage than that found experimentally by Drs. Weyrauch and Young.

In addition, we have studied two autopsy specimens by clamping the sigmoid above and below the site of the anastomosis and injecting methylene blue solution under considerable pressure. Reflux occurred in one of the four ureters.

The use of a tube of ileum or the isolated rectal bladder with an ileocolostomy above, offers some advantages in that it not only eliminates the hazard of intro-

during this period due to its lack of complete epithelialization acted as a point of entrance for infection and a focus of acute and chronic inflammation very close to the actual stoma of the anastomosis. Two clinical cases which we re-explored several months following Coffey 1 anastomoses for hydronephrosis showed identical nodules. This might well account for the late stricturing which occurred in some of the cases at the mucosal junction. Such an inflamed ureteral tip is an ideal site for producing ureteritis not only of the tip of the ureter but of the ureter within the sigmoid and above. Whether the ureteral tip sloughs promptly or not, in any particular case may be an important factor in accounting for the great variability in results which are obtained from one anastomosis to another. Several of our Coffey 1 dogs died of retraction of the ureter with leakage and peritonitis. This, we believe could have been prevented if sufficient length had been provided in the ureter and the tip had been more securely anchored. None appeared, however, to leak at the anastomosis.

With the end to side anastomoses of the Nesbit or Cordonnier type, no instances of retraction of the ureter occurred, due presumably to the fact that it was well anchored by the suture line. However, urinary leakage between the sutures was a prominent and disastrous complication. Attempts made to re-enforce this type of anastomosis with a second layer of sutures was only partially satisfactory. In animals that had no leakage, in many instances an excellently functioning anastomosis was produced, though again mucosal stenosis was found in some. Pyelonephritis, however, was a prominent occurrence even in several animals which had adequately functioning anastomoses. This probably is explained at least in part by the finding of reflux in more than half of the anastomoses tested. In cases where the stoma was not very adequate due to partial stenosis the chances of reflux were much reduced. The more adequate the stoma is, the greater the danger of reflux if no valve is present.

The portion of the ureter within the submucosal trough evidently is quite vulnerable to increases in bowel pressure which seem to effectively collapse it and prevent reflux. Both theoretically and practically the instance of pyelonephritis should be reduced if reflux can be prevented.

CONCLUSIONS

The ureteral tip following a Coffey 1 type operation does not slough promptly and may act as a source of acute and chronic inflammation at the site of anastomosis over a prolonged period, resulting in late stricture formation.

The end to side anastomosis is prone to leakage with acute and disastrous results.

Reflux has been found to occur in a considerable proportion of direct anastomoses.

A valve like action is obtained when the ureter lies in a submucosal trough, and reflux is prevented.

An anastomosis which combines a submucosal trough with a mucosal anastomosis avoids the main disadvantages of either the Coffey 1 operation or the direct anastomosis, and in our series produced results very superior to the other type of anastomosis.

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anastomosis, has devised his own method for uretero-intestinal anastomosis and thought it perfect, until a year or so after the operation. When he began to discover a delayed mortality in his patients, he gave up the method.

In searching the literature carefully, one has a difficult time finding a delayed report or a follow-up of cases two to five years after surgical intervention. Even though one succeeds in obtaining an ideal result and has an ideal operative technique, he still is faced with the problem of chemical imbalance, acidosis and reabsorption. Therefore, from my experience, which is much like that of many others, I still am not eager to recommend the transplant and cystectomy early. I withhold it until all other methods seem to fail, or until I am sure other methods will not control the lesion.

DR ROBERT E. JOHNSTON (Washington, D. C.) Uretero-intestinal anastomoses have been performed at Walter Reed Army Hospital by various methods, both experimentally and clinically, however, the best results have been obtained with a modified Coffey 1 technique. The essential feature of this modification is the use of polyethylene ureteral catheters secured to only one edge of the tip of each ureter by one plain catgut suture. This permits unobstructed drainage from each kidney both through and around a catheter. By the fourth postoperative day sufficient absorption of the plain catgut sutures has taken place to permit easy removal of the ureteral catheters. Using this method both ureters can be transplanted at the same time without fear of urinary obstruction during the early postoperative period.

Preoperative preparation consists of sulfasuccidine or sulfathiazine and high protein, low residue diet for five days, streptomycin for three days, insertion of a Miller-Abbott tube without suction two days preoperatively, and insertion of two rectal tubes just prior to operation.

The technique used is essentially a Coffey 1 method of uretero-intestinal anastomosis except for the following changes: 1) Both ureters are transplanted at one stage. 2) After division of the ureters a 6F polyethylene catheter is inserted up to each renal pelvis and secured by a suture of 00 plain catgut through only one edge of the tip of the ureter. 3) The left ureter is brought through the meso-sigmoid if it does not lend itself to transplantation readily into the recto-sigmoid in its lateral position. 4) Each catheter is passed through the bowel incision and each threaded into a rectal tube. 5) The anastomoses are accomplished using 00 chromic catgut atraumatic sutures throughout.

Postoperative treatment consists of aquacillin 300,000 units and streptomycin 0.5 gm. twice a day for 5 days, nothing by mouth for 4 days, Miller-Abbott tube drainage, proper parenteral fluid and electrolyte therapy, and removal of both ureteral catheters, one rectal tube and the Miller-Abbott tube on the fourth postoperative day. Rectal tube drainage is constant for one week and then gradually from 8 p.m. to 8 a.m. for an additional week.

This procedure has been used in 6 cases of bilateral uretero-intestinal anastomosis in one stage since December 1949. In four of these cases total cystectomy has also been performed at the same operation. The preoperative and postoperative urograms will now be presented in three of these 6 cases.

(Slide.) This is the preoperative urogram of case 1, a 25 year old soldier with

4) A procedure combining the submucosal tunnel with anastomosis of mucosa-to-mucosa, as has been employed by Leadbetter. This is referred to as the combined technique (fig 3, B)

Forty dogs ranging in weight from 6.5 to 14.5 kilograms, without selection as to sex, litter, age, or type, were used to study bilateral one-stage uretero-intestinal anastomosis by the four methods. In order to provide adequate controls two types of implantation were used in each animal, one method being used on one side and another type on the other side.

Of 80 anastomoses performed, there were 21 Coffey 1, 19 Cordonnier, 20 direct, and 20 combined operations. The survival time ranged from 2 to 434 days, the average being 47.9 days. Thirty dogs died, the remainder were sacrificed.

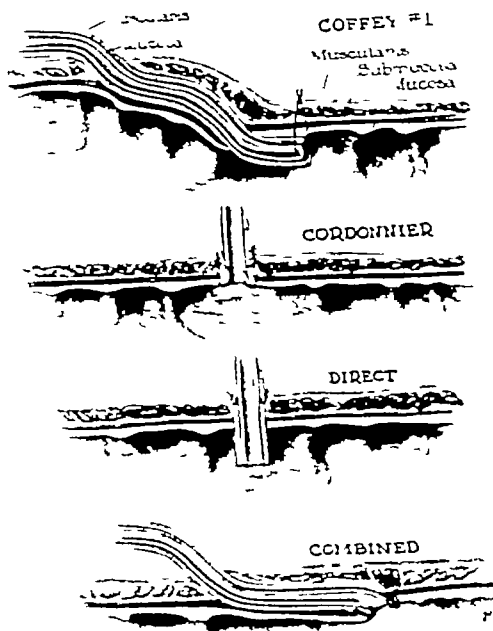


FIG. 1. Diagrammatic representation of four operative techniques.

When the dog died or was killed, all visceral organs were examined. Microscopic sections were taken of the kidneys, ureters, perirenal lymph nodes, lung and liver as well as of the spleen, heart, pericardium and peritoneum when indicated by gross examination. The sigmoid was tied off above and below the anastomosis; a ligature placed around each ureter in its lower third, and retrograde pyelograms made after urine had been aspirated for smear and culture. The lower and distal thirds of the ureters were injected with a solution of gelatin and India ink, fixed in 10 per cent formalin and cleared by the Spaltcholz technique.

In analyzing the results the four major complications of uretero-intestinal anastomosis were considered: reflux, leakage, obstruction and infection.

of the region of the ureter anastomosis with the incidence of obstruction and infection, because that may be an extremely important aspect of it, and the changes in that region of anastomosis may be upon the basis of infection or ureteral necrosis due to impaired blood supply.

I have two slides here which show another factor which may be of importance.

(Slide) In order to have a ureteral opening into the bowel which would be as near normal as possible, we anastomosed the trigone to the bowel, not exactly as old Maydl did, but we did that upon the basis of maintaining the trigone with its nerve supply and blood supply intact by bringing the bowel to the trigone. In a series of five dogs, every anastomosis held, and there was no peritonitis or anything of that sort. However, two months later, there was in every dog—as you see here—(slide) hydronephrosis and infection. Apparently this was upon the basis of severe infection in the trigone and the region of the ureteral orifices. These were widely exposed to the bowel contents and this may have been an extremely important factor.

There is one other factor which I would like to ask about and bring out, and that is this. I have noticed, in comparing patients with uretero-intestinal implants that the kidneys in those cases in which pelvic exsiccation had been carried out—as compared with those cases where pelvic exsiccation had not been carried out—turned out better in spite of less meticulous anastomosis, due to the condition of the patient, and so forth, in some of these cases, and in spite of a variation in technique at the region of the anastomosis. We are carrying out a group of experiments and comparing the different types of anastomosis in animals in which the sphincters have been destroyed, so that the intracolonic pressure is less.

Maybe the bowel habits of these patients has something to do with some of their complications.

DR REED M. NESBIT (Ann Arbor, Mich.) If all patients after uretero-intestinal anastomosis were sick and died as a result of their anastomosis, *nobody* would ever attempt the operation now or in the future. We have all been led on to try to improve our techniques because, ever since Coffey's day, a certain number of patients remain completely well following uretero-intestinal anastomosis.

Our own experience disclosed to us that 20 per cent of our patients who were operated upon by the Coffey technique, the various types of Coffey technique, remained perfectly well, clinically, and those 20 per cent of cases that we investigated were demonstrated to have no hydronephrosis, and infection did not develop.

In an effort to eliminate the factor of obstruction, which we considered might have been the important factor, efforts were made to avoid stenosis. We felt that a direct anastomosis made possible by moderate chemotherapeutic agents might be the answer. We tried a direct anastomosis of various types. We felt that avoidance of stenosis by this technique could best be effected by producing a spatulated end of the ureter which would be anastomosed directly to the mucosa.

In our series of cases, both animal and human, we found that we did not find obstruction and our patients were remarkably free from hydronephrosis but

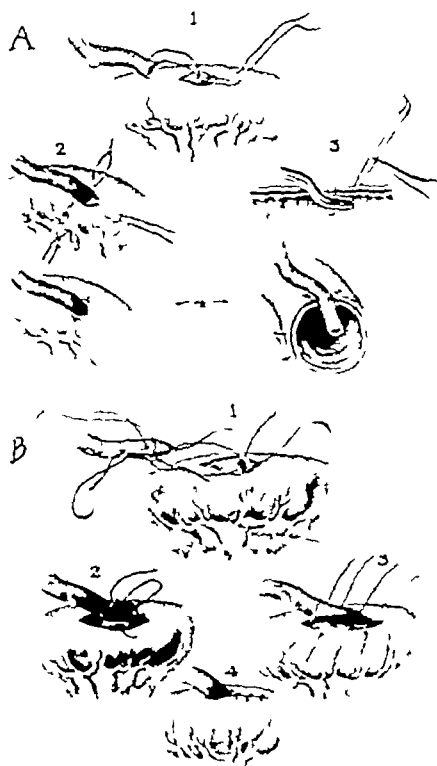


FIG 3 A, direct 1 Placing traction suture to draw ureter into bowel, 2, ureter fixed with sutures from adventitia to muscularis of bowel, 3, freeing intraluminal segment, 4, completed anastomosis

B combined 1 Placing mucosa to mucosa line of sutures, spatulate end of ureter slit proximally 2 union being completed, 3 formation of submucosal tunnel, 4, anastomosis complete



FIG 4 A gross specimen dog No 59 Right direct left Coffey 1 Dog killed 31 days postoperatively. Left severe hydronephrosis and severe pyelonephritis obstruction in part intraluminal segment and submucosal tunnel. Right mild pyelonephritis only, intraluminal segment of ureter sloughed

B retrograde pyelogram dog No 1 Right Cordonnier, left Coffey 1 Dog killed 59 days postoperatively. Right mild hydro-ureter and mild hydronephrosis. Left severe hydro-ureter and hydronephrosis

sults months after the implantation. This is an interesting technique, and one that is worthy of trial.

DR LORANDE M. WOODRUFF (Boston, Mass.) Dr. Leadbetter reported this combined method a year ago, and the series of clinical cases is rapidly increasing. Before very long there should be an adequate number of cases to give a thorough clinical evaluation.

As far as the blood supply of the ureter is concerned, although it is certainly of great importance, it did not seem to be the cause of failure in our dogs, with perhaps one exception. On the other hand we found in the Coffey 1 group that the blood supply at the tip was so satisfactory that it might continue to live for months.

I think there are many more difficulties relative to uretero-enterostomy that have not been taken up today, but these three or four points discussed seem of interest.

DR HENRY M. WEYRAUCH. Concerning the dog as an experimental animal, the one great difference between the dog and the human is that the dog's muscularis is much thicker than it is in the human being, and it seemed to us that if the dog's muscularis hadn't been so much thicker, with its grasping action upon the ureter, we might have had a higher incidence of reflux than we did.

Furthermore, because the muscularis is thinner in the human, and we have shown the submucosal channel affords protection, it would seem that there would be more likelihood of leakage in the human being than in the dog. As a matter of fact, I think we get more leakage following intestinal anastomosis than we suspect. In London last summer I was surprised to see Mr. John Sandrey drain the peritoneal cavity, following uretero-intestinal anastomosis. He said that urinary leakage frequently occurred, and he sometimes noted 200 to 300 cc from 48 to 72 hours after operation. I think we probably get it and do not recognize it before the anastomosis seals over.

We have found that the hydronephrotic ureter is really the dangerous ureter, and I think that is chiefly the question of blood supply.

Dr. Flocks asked about the implanted ureter. What takes place there is acute ureteritis, especially in the intraluminal segment, followed by gangrene. In some instances there is slough, but if there is not a slough, there is stricture formation. We published this in a previous paper on "The Destiny of the Implanted Ureter" (*Surg., Gynec. and Obst.* 74: 129-136, 1912).

As to the relative size of human beings and dogs, just a few weeks ago I was performing a uretero-intestinal anastomosis on a child of 18 months for exstrophy, and I was wishing then that I had a large dog upon which to operate.

in the table, which is a measure of the differences between the proportions, large values of chi square are associated with large differences and small values with minor differences. Calculations are made on the assumption that if the true proportions are equal, there is probability of obtaining a value of chi square as large or larger than the observed values. If this probability is small (0.05 or 0.01) the two proportions are considered to be significantly different.*

The calculated value of this probability in the current example is 0.01. The customary inference is summarized as follows: a significant difference exists in the true proportions among the four techniques at the 1 per cent level of signifi-

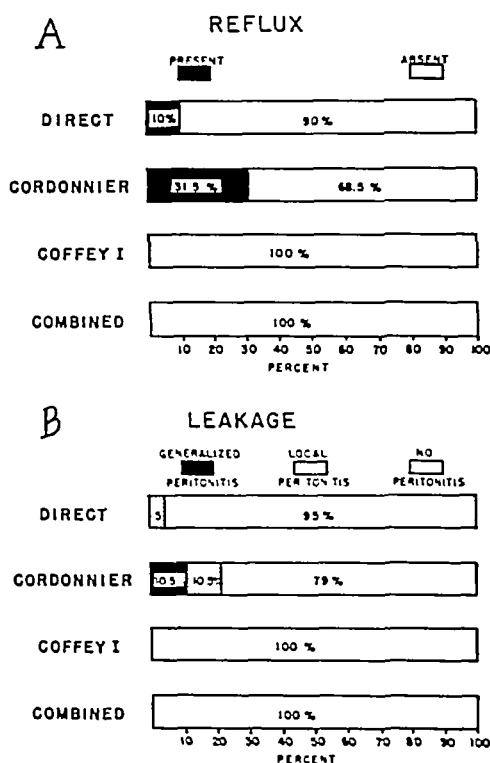


FIG. 6-1. reflux following various operations B, peritonitis following various operations

cance. Judging from the numerous instances of reflux following the Cordonnier, it appears likely that this operation has the highest true proportion of reflux. This is indicated by a comparison of the two methods without a tunnel, i.e., the Cordonnier and the direct, which shows a significant difference in the true proportion at the 5 per cent level.

Reflux occurred in 31.5 per cent of those ureters implanted by the Cordonnier technique and in 10 per cent of those by the direct method (fig. 6, 1). Since it was not observed following either of the tunnel operations, it apparently results

*Snedecor, G. W. Statistical Methods applied to Experiments in Agriculture and Biology. Ames, Iowa: The Iowa State College Press, 1940.

Two recent additions to our knowledge regarding these drugs have been made. The effect in delaying wound healing, due to the catabolic effect of cortisone on body protein has apparently been overcome by supplying extra protein in the diet, plus the administration of testosterone. The anabolic effect of testosterone on protein metabolism offsets, to some degree, the catabolic effect of the adrenal cortical hormones.⁶

The necessity for giving cortisone in intermittent courses with rest periods to enable the adrenal cortex to recover from the inhibitory effect of the hormone has apparently, been overcome.⁵ This has been done by taking advantage of the opposite effect of ACTH and cortisone on the adrenal cortex, cortisone depressing and ACTH having a stimulating action. It now appears that the two may be given simultaneously over weeks or months without the necessity of stopping treatment. This gives the prospect of more effective relief in conditions where long continued administration is desirable.

In our present study the effect of cortisone was studied on interstitial cystitis. The theoretical basis for a trial of cortisone in this condition was the belief that interstitial cystitis is a chronic inflammatory reaction involving mesenchymal tissues. Its similarity to lupus erythematosus was pointed out by Fisher,⁷ in 1938. Powell,¹⁰ in 1945, called attention to the factor of lymphatic obstruction, and Hand,¹¹ in an excellent summary in 1949, found that allergy was twice as frequent in interstitial cystitis as in a control group. Hand suggested the possibility of interstitial cystitis being an adaptation to various forms of stress. We do not feel that the exact etiology is as yet in view. Occurrence almost exclusively in the female and near or after the climacteric are presumptive evidence of an endocrine factor.

Sufficient cortisone was available* for trial in 6 cases of interstitial cystitis.

METHOD

1. Cases were screened for the well known contra-indications to cortisone therapy: diabetes, severe cardiovascular or renal disease and psychic instability.

2. During the period of administration the usual observations to detect untoward effects of the drug were made. Daily weight, blood pressure and routine urinalyses were done. Complete blood counts and Rindolph cosmophil counts were done at the start of therapy, 24 hours later, and then every 2 to 3 days.

3. The dosage followed was 300 mg. of cortisone the first day, 200 mg. the second day, and 100 mg. thereafter. Parenteral administration twice daily was used in the first series, and oral in subsequent groups. The cortisone therapy was preceded by a few days of placebo administration to evaluate psychic factors in the response.

Hoyt H. S., Doud, T. and Hoyt R. S. *Proc. Exp. Biol. Med.* **76**: 715, 1951.

⁶ Thorn, G. W. *Diagnosis and Treatment of Adrenal Insufficiency*. Springfield, Ill. Charles C. Thomas, 1949.

⁷ Fisher, G. M. *J. Urol.* **40**: 37, 1938.

¹⁰ Powell, Percy, *J. Urol.* **53**: 823, 1945.

¹¹ Hand, J. R. *J. Urol.* **61**: 291, 1949.

* We wish to express our thanks to Merck and Company for the cortisone used in these studies.

to an analysis of leakage, there was a significant difference at the 2 per cent level among the four techniques

Since leakage did not occur in the submucosal tunnel operations, it would seem that this complication is a defect peculiar to the insecurity of an axial implant. Closure of the muscularis over a submucosal channel protects the point where the end of the ureter joins or pierces the mucosa of the bowel. Although infection may spread along the course of the ureter this type of closure guards against peritonitis.

Figure 7, A provides the key for interpreting the various degrees of obstruction and infection which are depicted in the graphs which are to follow.

As concerns obstruction (fig 7, B), incidence was high when the direct transplant and the Coffey I were used and low with the Cordonnier and the combined. By grouping the methods with reference to common principles, statistical analy-

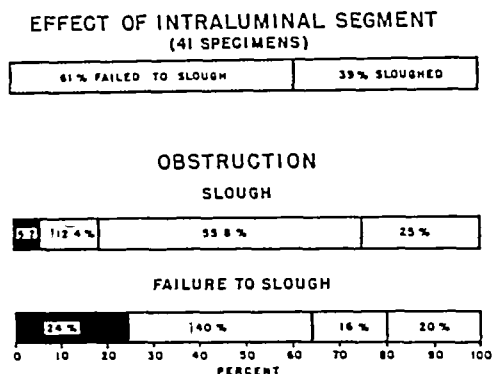


FIG. 8. Incidence of obstruction correlated with persistence of intraluminal segment

sis shows that in comparing the axial methods with the submucosal techniques (fig 7, C), there is no significant difference at the 5 per cent level. There is, however, a significant difference at the 2 per cent level in comparing the methods incorporating an intraluminal segment with those utilizing a mucosa-to-mucosa anastomosis. It would seem, therefore, that the submucosal channel is not an important factor, where the redundant ureter constitutes a potent source of obstruction.

More minute investigation of obstruction in the redundant ureter disclosed that the incidence was highest when slough did not occur (fig 8). After the intraluminal segment, next in order of frequency as causes of obstruction were constriction of submucosal channel, stenosis of sloughed stoma, stenosis of mucosa to mucosa union, intussusception, and no observable cause (fig 9).

The most common cause of obstruction, then, is infection which leads to ureteritis and stricture formation, especially in a persistent, devitalized ureteral stump. A vicious circle is initiated because obstruction caused by infection in turn produces increased infection. Where per primam healing almost never occurs when the anastomosis includes an intraluminal segment of ureter, the mucosa to mucosa union is conducive to per primam healing and to scaling off

ranted, not alone from the standpoint of therapy, but as a means of uncovering metabolic processes which may be related to the etiology of this distressing condition

ADDENDA

In his discussion of the foregoing paper, Dr. Robert Weaver of Salt Lake City called my attention to the fact that he had reported a series of cases of interstitial cystitis in which ACTH had been used. The results have been published in the Proceedings of the Second ACTH Conference.

In the symposium on interstitial cystitis at the 1950 meeting of the American Urological Association, during the discussion period Dr. John R. Hand made the suggestion that cortisone be tried in interstitial cystitis.

We have now treated two additional cases of interstitial cystitis with cortisone. The results have been essentially similar to the 4 cases reported in the foregoing text, with the exception that parenteral administration gave far greater relief than oral in the sixth case of the series.

Case 4 was later shown to have carcinoma. This was the only patient who did not obtain temporary relief from cortisone.

215 Franklin St., Monterey, Calif.

is that the intraluminal segment is undesirable, has no compensating virtue, and should therefore be abandoned. It constituted the most overwhelming cause of obstruction, contributed to a high incidence of infection, and provided no security against leakage or reflux. The surgical approximation of mucosa-to-mucosa was far superior in establishing a communication between the ureter and bowel. In eliminating most of the drawbacks of the intraluminal segment, this method afforded a better opportunity for healing.

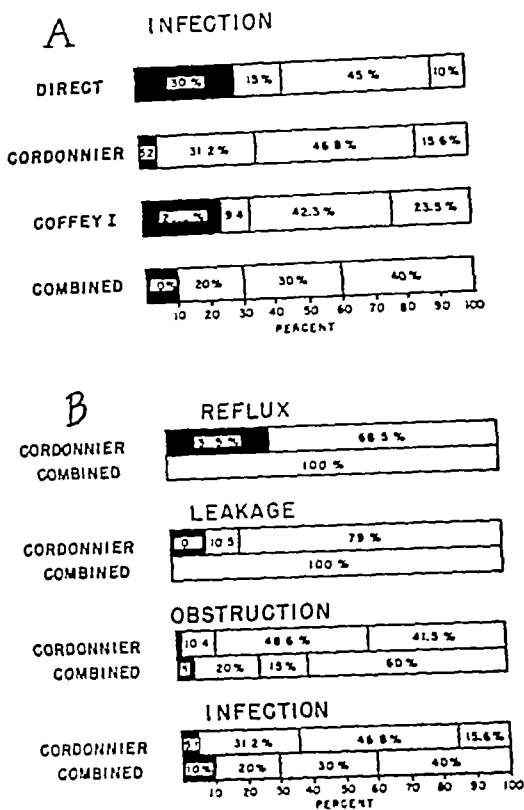


FIG. 10. A, infection following various operations. B, comparison of complications following Cordonnier and combined operations.

In abandoning anastomoses including the intraluminal segment, we are left with a choice between the two mucosa-to-mucosa implantations, one an end type, the other utilizing a submucosal tunnel. Leakage and reflux occurred only in the former (fig. 10, B), where as the incidence of obstruction and infection was approximately equal in both. The combined technique, therefore, proved most satisfactory in our series.

Before deciding to recommend the combined operation as superior to the Cordonnier, we tested another modification of the end implantation. An anchoring suture, similar to the one used in the Coffey I, was used to replace the apical suture of the Cordonnier. It was reasoned that invagination of the end of the

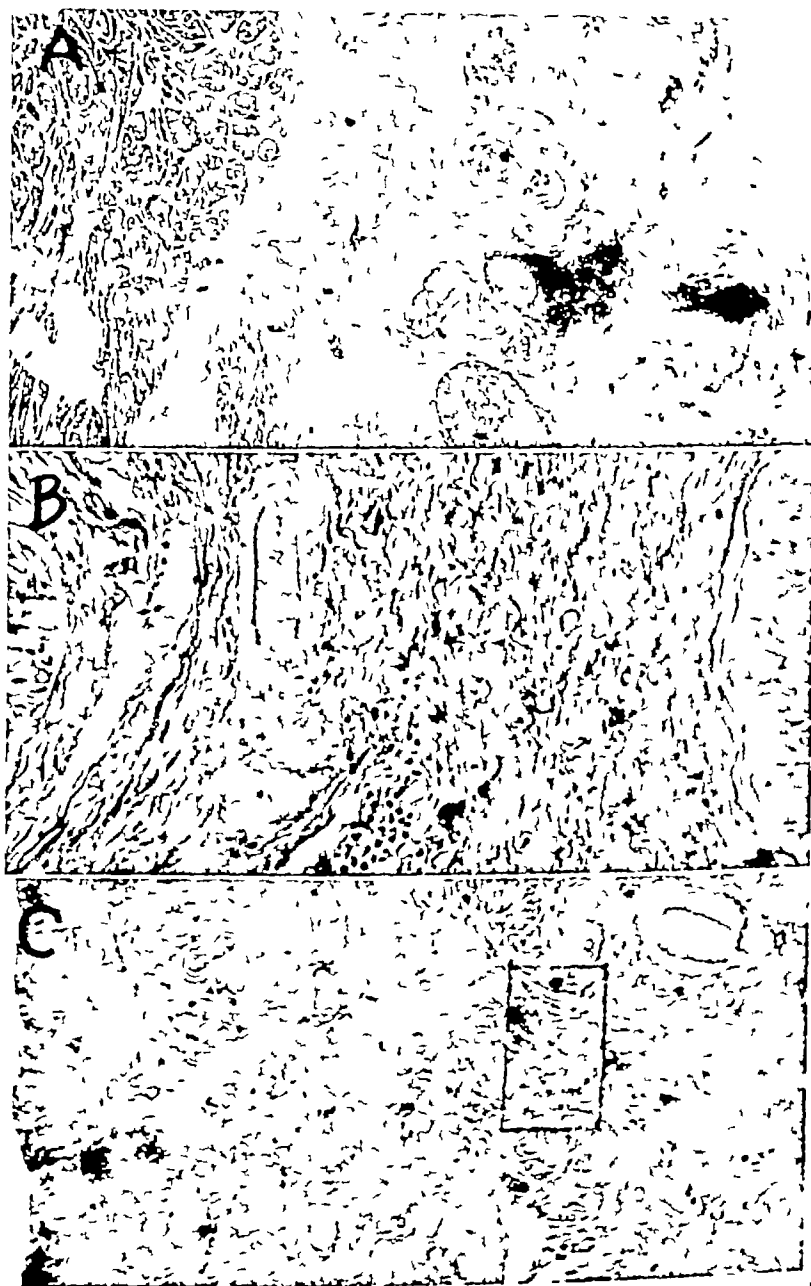


FIG. 1. *A* low power microphotograph of an area of interstitial cystitis removed from bladder showing crooked mucosa and submucous fibrosis $\times 30$. *B* high power microphotograph of lesion shown in *C* $\times 150$. *C* low power microphotograph of lesion removed by subtotal cystectomy showing pathology of interstitial cystitis $\times 30$.

and when these are seen lying beneath the normal epithelium near the ulcer, they at first suggest the picture of tubercle

against leakage and reflux, complications which are peculiar to axial implantation. Since an intraluminal segment leads to a high incidence of obstruction and infection without any compensating virtue, it is recommended that its use be abandoned.

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infection in this disease, for the condition is usually a "closed lesion" and infection might well be sealed within the bladder wall.

In spite of the suggestive but not very convincing evidence in favor of the infectious theory, interest in this explanation of the origin of interstitial cystitis has not been maintained. Furness, in discussing Bidgood's paper, said that in his experience [which was considerable, G. G. S.] the removal of infectious foci had never produced good results in this condition.

An even more weighty argument against the theory that infection is a principal cause of interstitial cystitis is found in the failure of these cases to improve in this era of "miracle drugs." Some patients—and some doctors—have reported improvement after the administration of sulfonamides, but in my experience the good effects have been transitory.

So far as is shown by a search of the literature, there have been only two well thought-out attempts to discover by experimentation the cause of interstitial cystitis. In 1937 Herbst (R. H.), Baumrucker and Germann reported an attempt to produce in dogs' bladders lesions comparable to those found in interstitial cystitis. In 15 female dogs adhesions were produced between the bladder and the internal genitalia by scarification, in some the "vessels" of the bladder wall were ligated. Lesions were produced which both cystoscopically and pathologically closely resembled the lesions of interstitial cystitis.

In 1945, Tracy O. Powell reported his "Studies on the Etiology of the Hunner Ulcer." Powell had laid the foundation for these studies by work which he published in *Surgery, Gynecology and Obstetrics* for 1944 on the lymphatics of the female urinary bladder. He found that "the lymphatics of the entire anterior wall of the bladder are drained chiefly by the union of many collectors into a large single trunk, of which there is one descending on each side of the bladder near the obliterated hypogastric vessels and proceeding down along the uterus over the uterine vessels to the primary lymph nodes." Obstruction to the drainage of these main collectors, he postulates, causes a blockage of the flow of lymph, and since there is little or no anastomosis between the lymphatics of the two sides of the bladder, there is a stagnation of lymph and even a retrograde flow in the area affected. Bacteria may be carried to the poorly drained area by this retrograde flow. Among the causes of blockage Powell enumerates the following:

"1) Blockage of a large number of lymph nodes by infection

- a) Pelvic inflammatory disease now or at some time in the past (specific or nonspecific)
- b) Various types of inflammation as a result of normal or abnormal parturition, abortion, ovarian disease, chronic cervicitis, etc.
- c) Infections in the cul-de-sac, retroperitoneal from pericystitis, etc., peritonitis and proctitis
- d) Typhoid fever and other diseases that are known to attack lymph nodes

2) Interruption of lymph circulation by tumors, such as fibroids and other pelvic surgical diseases

unal reflux, but solves the very troublesome problem of acidosis as well. At present, we are attempting to build up a series of patients on whom this modification is done and hope to submit a report of the results at a later date. The principal objection seems to be that either procedure adds considerable surgery to an already long and difficult operation, and will undoubtedly increase the operative mortality to some extent.

I shall await with interest a clinical trial of the methods presented. I believe we have made a great deal of progress in improving the technique of uretero-sigmoid anastomosis. However, I am not nearly so optimistic as regards our cancer surgery. Perhaps, with improved means of diversion of the urinary stream, we will feel more free to recommend cystectomy in earlier cases of vesical cancer, and thereby improve our results.

DR CARL A. WATTENBERG (St. Louis, Mo.) We have just heard an interesting evaluation of different methods of uretero-intestinal anastomosis from an experimental point of view. This subject has been of such importance that its various methods have been discussed for many years. Drs. Weyrauch and Young have made some thought-provoking conclusions. However, one might want to question the operative technique and results of surgery performed on a dog's ureter as compared to surgery performed on a human ureter.

This experimental study dealt with the four common hazards of uretero-intestinal anastomosis: peritonitis, ascending infection, obstruction to upper urinary tract, and reflux to the kidney. Four types of procedures or techniques were included in this experimental study.

(Slide) In a tunnel technique as shown in this slide, one can see what might happen if there is an undue reaction about the area of anastomosis, thereby causing fibrosis—pinching off the anastomosis and causing a hydronephrosis or ureteral obstruction. This also can be caused by the surgeon's suturing too much or too tightly, or by trauma setting up a reaction which will end in scar formation.

(Slide) In 1945 I was using a technique which placed the end of the ureter in the bowel lumen. This in many cases proved hazardous. I soon gave up the method and found the cause of my difficulties. The protruded end usually had an inflammatory reaction about it which resulted in slough, obstruction, fibrosis or stenosis.

(Slide) This shows a post-operative result in a patient who died. The ureteral ends show slough, edema and reaction. When the ureteral end was opened, considerable redness and reaction was found in the lumen. Some specimens had the ends sloughed off and were stenosed.

Dr. Cordonnier's method, as discussed in this study, must be defended by himself, since I like many other urologists have devised my own method. By his method it is conceivable that there easily could be a leakage and resultant peritonitis or if it were sutured too securely there might result a reaction with obstruction or stenosis. In the study just presented, however, it appears as though the anastomosis area is too widely open and allows a reflux. I am eager to know Dr. Cordonnier's clinical findings.

Many a surgeon during the past 73 years or since the first ureterosigmoid

this condition was the deliberate formation of a vesicovaginal fistula. Law on Tait in 1870, suggested making a vesicovaginal fistula as a means of curing perforating ulcers of the bladder. Skene in 1878 advised this procedure for the relief of what he called "vesico-urethral fissure" and mentioned the names of half a dozen surgeons who had employed "vaginal cystotomy" for bladder drainage and rest. Quinby, in a paper on resection of the presacral nerve, speaks of a woman with interstitial cystitis who in 1929 had been given a vesicovaginal fistula to put the bladder at rest.

Hunner in his early communications advised resection of the affected portion of the bladder wall. For about a decade this operation was the most favored method of treatment, but as Hunner himself said, the incidence of recurrence of the lesion in other portions of the bladder constituted a strong argument against its use. Kretschmer in 1926 reported that in eleven patients whose lesions he had resected there were 50 per cent cured, 10 per cent improved and 40 per cent with recurrences.

Folsom, O'Brien and Caldwell, in 1940, described a much more extensive operation which they hoped would eliminate the possibility of recurrence, this consisted in performing a subtotal cystectomy.

I shall have something to say about this operation in the discussion of my own series.

When other methods of treatment have failed transplantation of the ureters into the sigmoid has sometimes been done. So far as I can learn, Counsellor was the first to do this. In 1937 he reported 5 cases, the earliest of which was operated on in September 1929. Lower in 1939 reported having done this operation. Higgins advises it if other methods of treatment fail to give relief. There is no doubt that diversion of the urine will relieve the symptoms of interstitial cystitis but until the late results of uretero-enterostomy show a much lower incidence of renal failure, one hesitates to employ this measure for a condition which in itself is not dangerous to life and which may be alleviated by persistent treatment involving little or no risk.

As an alternative to uretero-enterostomy Nesbit has suggested intercolateral cordotomy, in 1946 he reported 2 such cases. Although Francis Grant in 1931 reported a case on which in 1923 he had done this operation for bladder pain "probably due to ulcers of the bladder," I have found no other reported case until Nesbit's report was published. In discussing cordotomy for the relief of bladder pain, David Band says that "post-operative retention of urine is a common feature temporarily observed after this operation, and it is as a result of cystalgia and prolonged frequency of micturition the bladder has become contracted, it may be difficult to re-educate the bladder satisfactorily. On the other hand, in the absence of pain, physiotherapy and tidal hygiene may with the cooperation of the patient do much to restore a normal bladder function after a successful cordotomy."

The probability that cordotomy will relieve more or less permanently the symptoms caused by interstitial cystitis makes this operation perhaps a better choice than uretero-enterostomy. Further clinical experience will be necessary before the question can be satisfactorily answered.

leiomyosarcoma of the bladder, which shows a normal upper urinary tract. Bilateral uretero-intestinal anastomosis was performed December 20, 1949 and total cystectomy on January 3, 1950.

(Slide) This excretory urogram, performed 4 months following transplantation, reveals normal calyces, however, the pelves do show slight dilatations over the preoperative film.

(Slide) This excretory urogram made after 6 months reveals little change.

(Slide) This is the preoperative excretory urogram of case 2, a 74-year retired soldier with a grade 2 papillary transitional cell carcinoma of the bladder, which shows some hydronephrosis and hydro-ureter on the left. Bilateral uretero-intestinal anastomosis was performed September 27, 1950 and total cystectomy on October 17, 1950.

(Slide) A urogram made 34 days following transplantation demonstrates marked improvement over the preoperative x-ray.

(Slide) This urogram, after 3 months, reveals mild hydronephrosis on the right and about the same degree of involvement on the left as seen prior to operation.

(Slide) This preoperative normal retrograde urogram is that of case 3, a 63-year old retired soldier with grade 2 papillary transitional cell carcinoma of the bladder. Bilateral uretero-intestinal anastomosis and total cystectomy were performed March 9, 1951.

(Slide) This excretory urogram performed 1 month after operation shows only moderate bilateral hydronephrosis.

The modification of the Coffey 1 technique described in this discussion has proved to be the most satisfactory method of uretero-intestinal anastomosis performed at Walter Reed Army Hospital.

DR. RUBIN H. FLOCKS (Iowa City, Iowa): The essayists have demonstrated many of the fundamental principles underlying successful uretero-intestinal anastomosis.

However, they have possibly—in their desire to emphasize the question of the mode of anastomosis—neglected somewhat the tremendous importance of the ureteral blood supply, the meticulous handling of the ureter, and the necessity of bringing the bowel to the ureter and fixing it there so that later tension upon the region of the anastomosis with the production of ischemic necrosis will not occur.

I believe that these are extremely important factors for the success of any type of uretero-intestinal anastomosis.

I believe, for example, that the reason that the intraluminal portion of the ureter causes difficulty is primarily on the basis of this lack of blood supply, and for that reason we have been avoiding this for several years with the performance of one or two stage anastomosis. We have found that it is not necessary to keep the intact ureter, as I originally thought, in order to maintain its blood supply. By meticulous handling and by a study of the ureter before anastomosis, you can tell whether there is an adequate blood supply, and you can anastomose at that point in the ureter where there is an adequate blood supply.

I am hoping the essayists if they could correlate the histological appearance

Transurethral Methods of Treatment

The transurethral fulguration of bladder tumors by Edwin Beer (1910) probably stimulated the application of this modality in the treatment of Hunner's ulcer. To my knowledge the first reference to the use of the fulgurating electrode in this condition was in the discussion of Hunner's paper in 1911 where it was stated that Arthur Chute had used this method.

Kreutzmann in 1922 published a paper entitled "The Treatment of Hunner Ulcer of the Bladder by Fulguration" in which he reported a case so treated by him in 1920. Pain was relieved but the bladder capacity continued to be very much reduced (145 cc). In the discussion of this paper Bransford Lewis said he had used fulguration in several cases but found the condition "rebellious." Buerger fulgurated a bleeding ulcer in one patient with cessation of the bleeding.

Frontz in 1928 said that of 26 cases of interstitial cystitis treated at the Brady Urological Institute within the preceding 5 years, fulguration was used in 5. He stated that the method was useful only in superficial lesions and advised resection of the affected portion of the bladder wall if fulguration was not effective. For the past 20 years fulguration has been employed as one of the accepted methods of treatment.

Overdistention of the bladder, usually with the patient under anesthesia, is also generally employed along with fulguration. Bumpus was apparently the first to comment upon the value of this procedure. His article appeared in 1930.

It is not clear to me exactly why fulguration and overdistention of the bladder relieve the symptoms of interstitial cystitis as completely as they frequently do. When one considers that the lesion often involves the entire thickness of the bladder wall and consists of a dense fibrous layer binding the mucosa to the musculature, why should a superficial destruction of the mucous membrane plus overdistention give so much relief of pain and an increase in bladder capacity sometimes amounting to a hundred per cent?

The relief of pain may be due to destruction of the nerve endings in the ulcerated area, the injection of absolute alcohol into the area of the ulcer probably produces the same effect.

I have not infrequently observed a one hundred per cent or greater increase in bladder capacity in the first few weeks following overdistention and fulguration. A good part of this increase can be maintained if the bladder is dilated to the point of tolerance at frequent intervals, perhaps once a week. It is difficult for me to believe that the initial overdistention in the anesthetized patient can produce changes in the bladder wall of such type and degree as to bring about so great an improvement so quickly. It seems more probable that the increased distensibility is due to the effect of fulguration upon the ulcer itself and upon the inflamed and over-sensitive nerve endings.

The superficial ulceration produced by fulguration heals as a flat, white cicatrix which, like all scars, is poorly supplied with nerve endings. The fact that irritations of redness may develop at the edge of the cicatrix and behave like typical Hunner ulcers while the cicatrix itself remains white, insensate and firm appears to support this theory.

they were not free from morbidity after operation. We continued to have a problem of morbidity, and we demonstrated in our own cases, both animal and human, that reflux did occur. However, there still was a significant number of patients who were completely well following this method of anastomosis, and it seems to me that our problem is related to finding out what factors contribute to the production of these well patients.

If we can avoid ascending infection and at the same time avoid obstruction, perhaps we will be closer to the solution of the problem. Perhaps we will never be able to produce a hundred per cent good results. I think, however, that the elegant experimental work described this morning by Drs. Woodruff, Cooper and Leadbetter may lead us a long way to the solution of this problem.

We are now performing the operation that they have suggested, utilizing the tunnel technique with the direct anastomosis, mucosa-to-mucosa. In effecting the direct anastomosis, I believe that we will prevent stenosis in the majority of cases if we will use the spatulated end of the ureter which the plastic surgeons have advised us to use, rather than using just the transected ureter stoma itself. We then have a stoma, you know, that is more than three times the diameter of the ureter itself.

DR M. LEOPOLD BRODNY (Boston, Mass.) I wish to congratulate the authors of the papers on uretero-intestinal anastomosis for their critical presentations and their excellent experimental studies. However, listening to the debate as to the merits of their various methods, I felt obliged to describe a technique which Prof. Alonso de la Peña demonstrated to me in Madrid several weeks ago, and which is performed without surgical anastomosis and without sutures. This operation was evolved because it was felt that sutures were an important factor in the production of ureteral stenosis at the site of anastomosis.

The procedure is very simple, and is as follows. The surgeon prepares a long silver wire which has a point on one end and a blunt tip of the approximate caliber of the ureter on the other end. A polyvinyl tube of the same circumference is obtained; one end is slipped on to the blunt end of the silver wire, and the other end is tied by a silk suture into the opening of the lower segment of the ureter. This silk suture is left long and is carried down to the pointed end of the silver wire. The ureter may be inserted at any place in the bowel that is most convenient. This has the advantage of preserving the blood supply to the ureter, and not disturbing it from its bed to any extent.

An assistant manipulates a sigmoidoscope which has been passed up the bowel so that the surgeon can see the light of the open end of the instrument. The sharp end of the silver wire with the long end of the silk suture is passed right through the wall of the bowel and guided into and through the sigmoidoscope until it reaches the distal end. Continued pull brings the polyvinyl tube through the wall of the bowel. This is continued until the entire tube and approximately 2 cm. of the ureter projects into the bowel lumen. Slight tension is placed on the silk suture outside the rectum to prevent the ureter from pulling away. The ureter remains so constant drainage until about the tenth day when the suture sloughs. The polyvinyl tube is passed out of the rectum.

The course of the postoperative pyelograms and they showed excellent re-

at least one year. Actually there was only one case in which the duration of "cure" was under two years, this patient died following an operation for gall bladder disease after having been free of bladder symptoms for 1½ years. Most of the patients listed as "apparently cured" were found to have bladder capacities of at least 300 cc or reported by letter or telephone that they had no urinary symptoms. One woman over whom I had labored faithfully but had not seen for several years, told me when I called her to inquire as to her condition that she was "perfectly well and had been since she had stopped taking fruit juices."

The longest period of freedom from bladder trouble recorded in this group was 13 years. This patient was first seen by me in 1926. She was 46 years old and had had urinary symptoms for about one year. Cystoscopy showed 5 or 6 very red areas which cracked and bled when the bladder was distended to 120 cc. A culture of the urine and a guinea pig inoculation were both negative. She was treated by dilatation and fulguration in the office for three years with temporary relief, it was not until she had thorough fulguration under anesthesia that real progress was made. I have not seen her since 1930 but by telephone I learned that, except for one period of bladder trouble in 1938, she has been entirely free of bladder symptoms (1951).

Group 2 Improved but still under treatment, 14 cases. This group includes patients who have been under treatment for at least 2 years, 8 have been under treatment for at least 5 years. The longest period was 23 years. The patient with this record I now see every few years, the last time in 1950. Her bladder holds 240 cc with discomfort, frequency of urination averages every 2 hours by day and 2 to 3 times at night. Cystoscopy shows the mucosa to be generally congested and the capillaries more dilated than is normal. No areas characteristic of interstitial cystitis are seen. The patient, who is a model of fortitude, says she is free from pain and is "well adjusted" to her urinary frequency.

Six other women have been kept comfortable by dilatation of the bladder every month. One of these kept up this treatment until her death 10 years later. Several others do well under this treatment for months at a time but now and then develop new ulcers which require fulguration.

Group 3 Women who ceased treatment before the final outcome was determined, 18 cases. Fifteen of these patients were improved by treatment varying from a few visits to visits extending over two years. Three did so well that it seems not unlikely that they may have been cured.

Group 4 Women who were not helped by treatment, 4 cases. One was not improved by previous treatment given by Dr. Furness and four treatments given by me.

One developed an hourglass bladder due to contraction of the scar of the interstitial cystitis. Her ulcers had been fulgurated twice.

One had not improved by 3 years' treatment, in which the silver nitrate method was used.

A fourth became "worse than ever" after resection of a Hunner ulcer, it is probable that the resection was not sufficiently extensive.

From a review of these 49 cases, it appears that fulguration should have been

CORTISONE IN UROLOGICAL CONDITIONS WITH A REPORT OF A TRIAL IN INTERSTITIAL CYSTITIS

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Cortisone and ACTH have now been used in a wide variety of conditions. In many cases the response has been dramatic and in an additional group, marked benefit has been obtained. A survey of the work to date reveals that in the field of urology these compounds have apparently not yet been given the trial they merit. In order to ascertain what urological conditions might be benefited by cortisone or ACTH, a review of the physiological action of these hormones is indicated.

Selye¹ was perhaps the first to recognize that the stress of various kinds of trauma, both physical and psychic, infection, burns and injury, incites a common type of defense reaction on the part of the body.

Later an additional concept was introduced which recognized that this defense response might be so excessive that it would in itself be harmful, even after the primary stress had been successfully overcome. It is not the irritant, but chiefly the tissue reactions to the irritant, which constitute the 'disease'.^{2,3}

In addition to the inhibition and, at times, dissolution of mesoblastic and lymphatic tissues, cortisone has many other metabolic effects. Among them are: 1) depression of circulating eosinophils, 2) tendency to force protein into carbohydrate (gluconeogenesis in liver), 3) lowers the gamma globulin level in blood, 4) increases need for insulin in diabetes, 5) increases excretion of uric acid, 6) may show tendency to salt and water retention and loss of K, 7) may produce rounded face, hirsutism and virilism (Cushing's syndrome).

In acute infections cortisone may have a direct antitoxic action. In pneumonia⁴ the temperature may fall within 24 hours, whereas the blood culture remains positive and the lung consolidation unchanged. This would seem to indicate neutralization of toxins, the causative organism remaining unaffected. A tremendous amount of experimental work has been done recently to appraise the effect of cortisone in acute bacterial and viral infections. Reported results are somewhat contradictory.⁵ Current opinion indicates that in the following four conditions, cortisone or ACTH is mandatory: 1) general peritonitis,⁶ 2) acute infections not responding to antibiotic therapy, 3) acute inflammations of the eye, 4) burns and other forms of shock.

Read at annual meeting Western Section, American Urological Association, San Valley, H.P., June 27, 1951.

¹ Selye H. *J. Clin. Endocrinol.*, **6**: 117, 1946.

² Herch P. S. *Proc. Staff Meet. Mayo Clinic*, **25**: 475, 1950.

³ Finland M., Koss I. H. and Ingbar, S. H. *Proc. of the First Clinical ACTH Conference*, 1950, pp. 24-35.

⁴ Koss I. H., Ingbar S. H. and Finland M. *Ann. Int. Med.*, **33**: 1051, 1950.

⁵ Koss I. H. and Finland M. *N. Engl. J. Med.*, **244**: 464, 1951.

⁶ Koss I., Laurence W. and Marken Sheldon. Unpublished data.

in the bladder wall. In the majority of cases, the bladder wall was smooth, the mucosa pale. Upon dilatation with the patient under anesthesia, numerous delicate fissures developed over most of the fundus or tiny bleeding points appeared, dilatation of the bladder by a hydraulic pressure of about 3 feet of water (90 cm) failed to increase the bladder capacity by more than 75 or 100 cc.

The men with interstitial cystitis were treated by bladder dilatation, usually in the office and without anesthesia. In 3, localized areas of interstitial cystitis (Hunner ulcer) were electrocoagulated.

In one patient, a man with unbelievable frequency of urination—60 times in 24 hours—the ureters were transplanted to the sigmoid. The right ureter was transplanted in July 1945, the left in July 1947. Ten months after the second operation the patient died, probably of pyelonephritis.

As to the results obtained in this group of 15 men, 3 were much improved, 3 were moderately improved, and 2 slightly improved. Seven did not follow treatment long enough to give it a fair trial.

DISCUSSION

It is my present belief that cases of interstitial cystitis should be treated by fulguration and dilatation done under general or spinal anesthesia, and should be followed by regular dilatation at least once a month and at times more frequently. The good results obtained in 16 of my 64 cases indicate that interstitial cystitis does not offer an insoluble problem. If the disease continues to be limited to one area and does not yield readily to treatment, I think that wide resection of the affected area should be carried out. The results which followed one of my two resections and a number of those done by Hunner, Hunt, Kretschmer and others leads me to this conclusion.

SUMMARY

The pathology and etiology of interstitial cystitis are discussed.

Methods of treatment are outlined: surgical, transurethral, systemic.

A summary of the results obtained in 49 women and 15 men is given. Thirteen of the women were cured, many of the others were improved. Four women were not materially improved after adequate periods of treatment.

I wish to express my indebtedness to Dr. Wm. A. Meissner for the excellent microphotographs presented herewith.

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4 Observations recorded were

I Objective

- Bladder capacity before and after therapy
- Degree of cracking and bleeding of involved area

II Subjective

- Degree of pain
- Number and interval of night voidings

TABLE 1 *Effect of cortisone therapy on Hunner's ulcer of the bladder*

GROUP I 4 cases—1 course—10 days

CASE	AGE	SEX	DURATION OF SYMPTOMS	PREVIOUS TREATMENT	BLADDER CAPACITY		BLEEDING ON DISTENSION†		DEGREE OF PAIN		NYCTURIA			RESULTS
					Before	After	Before	After	Before	After	Be-fore	Af-ter	1 Mo. Later	
					Cortisone	Cortisone	Cortisone	Cortisone	Cortisone	Cortisone	Cortisone	Cortisone		
1	65	F	30 yr	F D	500 cc	640 cc	++-	±	0	0	4	2	1	Partial relief of nycturia—no pain in this case
2	60	F	14 yr	P	200 cc	200 cc	++-	±	+++	++	S	4	6	Temporary partial relief of pain
3	75	F	15 yr	P F D	200 cc	210 cc	++++	±	++++	++	S	7	See foot note	Temporary partial relief of pain
4	65	M	1 yr		100 cc	180 cc	++	++	++	++	6-S	6-S		Poor

* P—Pool treatment—Gradually increasing strengths of silver nitrate instillations with distention

F—Fulguration

D—Distention

† As observed cystoscopically

SUMMARY Objective findings Marked reduction in "splitting and bleeding" in all four cases

Subjective findings Partial temporary relief of pain in the 3 cases presenting pain as a symptom

6 cases—2 mos. after treatment still about 50% relief of pain

RESULTS

The results are summarized in table 1

Exact control has been very difficult. Most of the patients reported some relief from the placebo medication. The cystoscopy just before treatment doubtless showed some relief, due to the coincident bladder distention. This factor is being controlled in cases at present under study.

CONCLUSION

No firm conclusions are possible from this preliminary study. Cortisone seems to have a beneficial effect in interstitial cystitis. Further investigation is war-

RADIOCOBALT IN THE TREATMENT OF BLADDER TUMORS

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The technique of using radioactive cobalt beads for intracavitary radiation of bladder tumors was first suggested by one of us (BVAL-B) in January 1946. The following reasons argued for a trial of this technique: dissatisfaction with the results of radical surgery and of conventional radium, radon seed, and external x-ray radiation, certain physical advantages of radiocobalt over radium, availability of radiocobalt beads.

Dissatisfaction with other methods of treatment of bladder tumors is not limited to this clinic. A recent review of cases of radical cystectomy from the private hospital affiliated with the University of California showed only 3 possible cures among 23 patients. In one of these the neoplasm was shown to have been removed completely by the preliminary transurethral resection. Radon implantation had been tried and abandoned. External high voltage, and low voltage contact x-ray therapy were disappointing in therapeutic effects, and caused contracted bladder, and occasionally ulceration of the rectum.

Radiocobalt has certain physical advantages over radium (fig 1).

1) The metal cobalt may be made safely into convenient beads of any size and shape before it is activated.

2) Cobalt can be made radioactive to any desirable strength.

3) The undesired beta radiation has the low energy of 0.3 mev and is easily screened by 0.1 mm thick silver plating. Radium requires more filtration because of higher energy beta radiation.

4) The gamma radiation, upon which the therapeutic effect depends, is almost monochromatic, with a mean energy of 1.2 mev, while radium gives off more heterogeneous gamma rays, with a mean energy of 0.8 mev.

5) For equal dosage units 1 millicurie of Co^{60} approximately equals 1.65 milligram of radium.

6) Radiocobalt ($^{60}_{27}\text{Co}$) decays to the stable element nickel ($^{60}_{28}\text{Ni}$), whereas radium ($^{226}_{88}\text{Ra}$) disintegrates through a whole series of radioactive daughter products into the stable element lead ($^{206}_{82}\text{Pb}$).

7) The one disadvantage of radiocobalt is its shorter half-life (5.3 years) as compared to radium (1680 years).

Radiocobalt was available as it had been developed and used in a series of nasopharyngeal tumors by Morrison.¹ An inadequate supply of radium had stimulated him to find a radioactive isotope with metallic physical properties, and adequate half-life. Radioactive cobalt met these requirements. Details of metallurgical preparation of the cobalt beads and their activation in the nuclear pile at Oak Ridge are contained in his paper.

Read at annual meeting Western Section American Urological Association, San Valley, Idaho, June 27, 1951.

¹ Morrison, L. F. Arch Otolaryng, 53: 153-155, 1951.

INTERSTITIAL CYSTITIS

GEORGE GILBERT SMITH

Interstitial cystitis is today a well-recognized bladder lesion, at least by urologists. The symptoms are characteristic. The bladder capacity is reduced sometimes to as little as 100 cc. When the bladder is distended above a given amount, the patient suffers intolerable pain. If distention is carried above this point, bleeding may occur from fissures which develop in the affected area. Some patients complain of a constant pain which is most frequently referred to the suprapubic area and is sometimes located more to the right or left according to the position of the lesion in the bladder. In a typical case urinalysis shows no pus or bacteria but there may be a few red blood cells and a very slight trace of albumin.

Although Skene used the term "interstitial cystitis" in the 1887 edition of his *Treatise on Diseases of the Bladder and Urethra in Women*, the condition which he described does not resemble the one with which we are concerned. Nitze, however, in the second edition of his *Lehrbuch der Kystoskopie* (1907) described a typical case of interstitial cystitis and gave the condition the name of "cystitis parenchymatosa." "Pannural cystitis" and "submucous fibrosis" are terms used by later writers to describe this lesion.

PATHOLOGY

On November 13, 1914 Guy Hunner read before the New England Branch of the American Urological Association a paper entitled "A Rare Type of Bladder Ulcer in Women." His description of the cystoscopic appearance and the pathology of this lesion has never been improved upon and is accepted by practically all of those who have since then written on this subject. Hunner wrote:

Microscopically one finds in the resected portion of the bladder wall a typical picture of chronic, simple ulcer. The epithelial layer is absent at the site of the ulcer and the mucosal layer is occupied by typical, chronic granulation tissue. In some of the specimens this granulation tissue is fairly richly supplied with capillaries, but in most of them there is a preponderance of connective tissue and infiltration of small round cells and leucocytes.

The epithelial surface in the neighborhood of the ulcer shows multiple layers of the transitional type of cells, the external layers being of the squamous stratified type and in places appearing hornified. Next to the ulcer the epithelial layer may end abruptly with a precipitous edge or there may be seen extending beyond this abrupt edge in attempt at repair in the nature of a single layer of cuboidal cells growing toward the bare surface of the ulcer.

The mucosal layer in the neighborhood of the ulcer shows an increase in the number and size of the capillaries, varying in the different specimens. The capillaries are often stuffed with leucocytes as are many of the lymph spaces. There are some enlarged lymph spaces crowded with lymphoid cells and leucocytes.

1. First annual meeting, American Association of Genito-Urinary Surgeons, Sept. 13, 1931, p. 161.

between source and tumor, greater relative depth doses can be attained. This facilitates the delivery of high doses to deep seated tissues without producing necrosis of tissue surface.

The effective tissue dose is due to absorption of the radiation by the tissues. Since the energy absorption in air closely parallels that in tissues for the high energy cobalt gamma rays, in clinical practice there is very little difference in the dose at a given point in tissue and in a corresponding point in air within a radiation source-tissue distance not exceeding 4 cm. A balloon distended to 50 cc has a diameter a little over 4 cm. Figure 3 shows the millicurie hours necessary to produce 1000 roentgen γ at various cobalt-tissue distances.

TECHNIQUE OF APPLICATION

Originally the radioactive cobalt bead (0.3–0.5 mm in diameter) was placed in the central channel of a Foley or Foley-Alcock type catheter in such a position

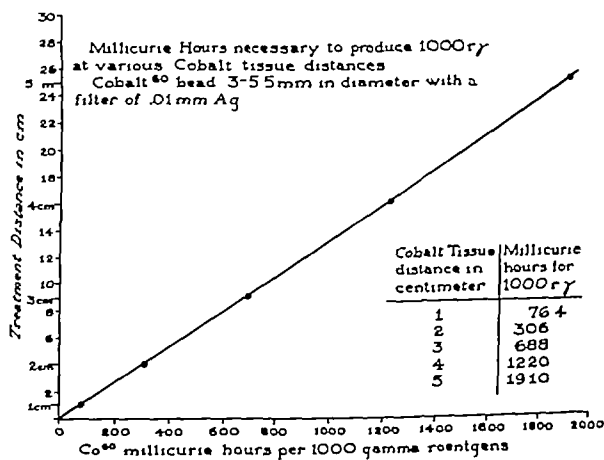


FIG 3 Graph of dose distance relationships³

that when the Foley bag was inflated the bead was in its center. Such a catheter is used to insure uniform distribution of radiation. However, not all catheter bags are symmetrical, so that the symmetry of the bag must be ascertained by inflation prior to use.

Subsequently a home-made, then a manufactured* *special catheter* has been used to hold the bead and still permit the outflow of urine. This eliminated the cystostomy or large three-way catheter. Details, including a spherical 50 cc bag, built-in barrier for use of a stilet, and drainage holes at the base of the balloon, are shown in figure 4. The catheter is cold- or hot-sterilized after insertion of the bead through a distal opening. The balloon is tested for sphericity and leaks.

The procedure begins by inserting the catheter through the urethra, with or

* By the American Cystoscope Makers, Inc.

³ Low Beer, B. V. A. The clinical use of radioactive isotopes, American Lecture Series, No. 54, American Lectures in Radiation Therapy, Springfield, Ill., Charles C. Thomas, 1950.

There is hyaline degeneration in some areas and in some of the sections the edema causes rarification

'The muscle coat shows enlarged lymph spaces, and these, as well as some of the blood vessels of the muscle coat, contain many leucocytes. Immediately beneath the ulcer, the muscle in places shows invasion and breaking up by the inflammatory process.'

Hunner's communication was the first to describe the symptomatology, the cystoscopic appearance and the pathology of this condition (fig. 1) and to suggest a method of treatment. Since then, the term "Hunner's ulcer" has been in common use.

The extent of the changes in the bladder wall has been emphasized by Nitze, who found the entire thickness of the bladder wall to be involved within a circumscribed area. Kretschmer (1922) gave an excellent description of the pathological findings in an excised portion of the bladder wall and remarked that the enormous thickening of the bladder wall was out of proportion to the size of the ulcer itself. Hand, in studying the changes in the bladder wall, found in a case of interstitial cystitis, was impressed by the extent of nerve involvement as evidenced by edema and leukocytic infiltration about and within the nerve sheaths.

ETIOLOGY

Hunner's paper appeared at a time when metastatic infection from teeth and tonsils was thought to be a factor in many diseases. It was reasonable for him to believe that such foci were the cause of "elusive ulcer," as he called it. There has been evidence to support this theory in the work of Bumpus and Meisser, who in 1921 reported that they had produced lesions in the walls of rabbits' bladders by injecting into the circulation a *Streptococcus viridans* grown from the infected teeth of patients with interstitial cystitis. Winsbury-White in 1933 described experiments in which India ink injected into the uterine cervix appeared in the lymph spaces of the bladder wall. In my own series of cases with interstitial cystitis there was noted in two instances the occurrence of acute exacerbation of the bladder symptoms following the extraction of infected teeth. One of these patients has been greatly improved since seven infected teeth were removed some fourteen years ago.

Bidgood in 1928 cultured in a bismuth medium small pieces of bladder wall taken from the involved areas in two cases of interstitial cystitis in which the urine had been sterile, in both instances pure cultures of streptococci were grown.

Kretschmer has reported the results obtained by culturing sections of bladder wall removed from three of his cases. These results were inconclusive: colon bacilli were grown from one streptococci from another, a few colonies of staphylococci from the third. A section of bladder wall removed from one of my patients was inoculated and cultured, no growth was obtained.

The fact that in the large majority of cases of interstitial cystitis the urine is perfectly and usually free of pus does not of itself contradict the theory of metastatic

Dosage is calculated from the measured distance of tumor to bead, taking into account radiographic distortion. Our practice has been to give 6000 gamma roentgens at each insertion to the surface of the bladder, usually at a distance of 2 to 2.5 cm from the radiocobalt bead. Each exposure lasts about 100 hours. If one application is not sufficient (infiltrating tumor or lack of resolution after initial dose), a second application is given after an interval of from four to six weeks.

TABLE 1

PT	AGE	SEX	TYPE OF TUMOR	FOLLOW UP	REMARKS
<i>Papillomatosis</i>					
A M	66	F	Multiple benign?	Improved, small recurrence resected	Severe radiation cystitis
M O	70	F	Multiple benign	No improvement	No demonstrable effect on tumor
<i>Localized tumors</i>					
B Z	65	M	Malignant papilloma	Recurrence	No subsequent recurrence
G S	74	F	Malignant papilloma	Lesions are healed	Moderate radiation cystitis. Good result
F V	59	F	Malignant papilloma	Recurred	Ureteral transplantation
H O	69	M	Papillary carcinoma "Grade I"	Healed, no recurrence	Good result
J A	60	M	Papillary carcinoma "Grade I"	Developed 1 small recurrence	Some improvement

INDICATIONS FOR TREATMENT

On theoretical grounds, multiple papillomas without infiltration are ideal for treatment by intracavitary radiation, since fulguration and resection are often impractical and cystectomy too radical. We have also used cobalt therapy for single, superficially infiltrating tumors (Jewett's⁴ group 2A), as well as on advanced lesions.

IMMEDIATE REACTIONS

Reactions of the bladder wall to cobalt radiation appear to be somewhat less severe than with similar doses of radium or externally-administered x-radiation. Doses of 6000 roentgens produce erythema as seen by cystoscopy, the patient usually complains only of some burning and frequency of urination. The second exposure, for a total of 12,000 roentgens, however, gives a more severe reaction.

⁴ Jewett, H. J. *J. Urol.*, 67: 672, 1952.

- 3) Surgical interruption of collectors during pelvic operations
- 4) Blockage of anterior horizontal collectors
 - a By infection as a result of cervicitis, giving rise to supravescical fibrosis
 - b By possible pressure from uterus against pubic bone, interrupting rare type of main collector on anterior wall of bladder "

Powell advises that a Frei test be done on all cases, he had several patients in whom the test was positive. Powell says that "the histologic picture in the typical case of elusive ulcer is identical to an hypothetical case of chronic lymphatic edema in that area. Histologic sections of dogs' bladders with partial lymphatic obstruction [produced by the injection of thorotrast into the bladder wall, G. G. S.] were not unlike those in the majority of reported cases of elusive ulcer." Powell says in a paper published in July 1949, that early chronic lymphedema with subsequent fibrosis ultimately involves the parasympathetic nerve filaments, thus producing reflex spasm of the bladder musculature.

Powell's work on the etiology of Hunner ulcer is, in my opinion, most convincing. In one of the few instances in which I resected an area of interstitial cystitis, the edema of the affected area was clearly visible when the external surface of the bladder was exposed. Powell's theory gives a valid reason for the much greater incidence of this condition in females than in males. It explains why interstitial cystitis is most frequent among women of middle age. Bumpus refers to "the noticeable incidence of previous pelvic operations, especially of hysterectomy, among women who suffer from interstitial cystitis."

There is a question as to the existence of factors which predispose to the development of this disease. In my series of 49 women who were so afflicted, in over 40 per cent the symptoms appeared at or about the time of the menopause. It may be of some significance, though I do not know what, that over 50 per cent had never borne children. Kretschmer says that 5 of 13 of his female patients had never been mothers.

Another factor which is of interest has been suggested by John R. Hand. Hand reviewed the histories of 204 women and 19 men who had been under his care and compared their histories with those of an equal number of patients of the same age groups who were under treatment for some other condition. In comparing these two groups, Hand found "a higher incidence of allergies, gallbladder disease, cystoceles, pelvic operations and some types of toxic, among the patients with interstitial cystitis than among those in a group selected for comparative study." Hand found also that in many of his patients with interstitial cystitis were of a psychoneurotic type; he suggests that interstitial cystitis may be initiated by a neurologic factor.

Although Hand's work does not lead to definite conclusions as to the exact etiology of this disease, it does give valuable information regarding the secondary factors concerned in its development and chronicity.

TREATMENT

The treatment of interstitial cystitis may be classified as surgical, transurethral and medical. Perhaps the earliest surgical procedure employed for the relief of

Three cases are reviewed in more detail because they are representative of of the group as a whole

1 *Multiple papillomatosis* Mrs A M, aged 66, had known recurrent papilomas of the bladder for 15 years. These had been treated elsewhere by electrodesiccation as they recurred. When first cystoscoped here 18 months ago, her bladder mucosa was so studded with minute papillomas that no field could be found that didn't demonstrate 15 or 20. In addition, her bladder presented numerous scarred areas where the lesions had been previously fulgurated (fig 6, A). Accordingly, after study, she was given 6000 roentgens of radiation with radiocobalt. She was followed at bimonthly intervals for the next 3 months. She developed a rather severe radiation reaction characterized by an intensely red and edematous bladder mucous membrane, which, however, had largely subsided at the end of two months. At that time, it was noted that she still had a few

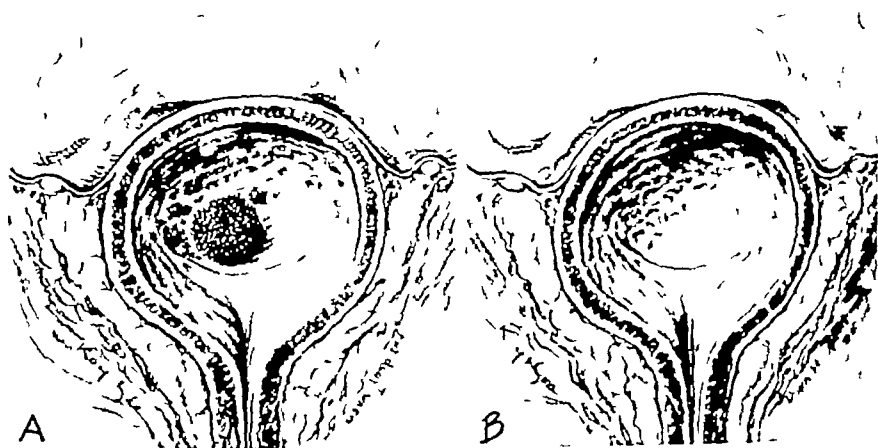


FIG 7 Malignant papilloma G S (female, aged 74) A, grade 1 malignant papilloma with tumors on right and previous resection on left B, good results 3 months later

tiny papillomas about the right orifice, and she was given a second 5200 roentgen radiation. The second exposure produced again a rather severe reaction, but within 2 months, no trace of papillomas could be seen (fig 6, B). She has been cystoscoped at 2 to 3 monthly intervals since. Probably as a result of a combination of radiation and previous fulguration, her bladder capacity is now only 100 cc and the epithelium is very sensitive and bleeds almost at the touch. In addition, 6 months ago she was found to have a small tumor near the right orifice, which on biopsy proved to be a malignant papilloma, and again two months ago, was found to have multiple recurrences. These were destroyed by fulguration since it is doubtful that her bladder could stand further radiation.

2 *Localized tumor* Miss G S, aged 74, was first seen almost 2 years ago, at which time she was found to have a single papilloma above and to the left of the left orifice. This was resected and the base fulgurated. The tissue diagnosis was "malignant papilloma." She was observed at regular intervals for one year

The first presacral neurectomy for relief of the pain of interstitial cystitis was done by Pieri in 1926 (Learmonth). In 1932, Learmonth and Braasch reported 24 cases, eight of which were done because of interstitial cystitis. Among these 8, there was no, or slight relief in 5, marked relief in 2, one had been done too recently to know the results.

Richer states that the presacral plexus does not convey sensation arising in the bladder wall, but is concerned only with sensations arising in the peritoneal covering of the bladder. Learmonth noted that when the presacral nerve was cut, there occurred dilatation of the vessels of the bladder mucosa, he believed that presacral neurectomy improved the nutrition of the bladder wall in patients with interstitial cystitis. Schroeder (1930) in patients with this lesion excised the presacral nerve and also the lateral sympathetic chains, if necessary he added intrathecal injection of absolute alcohol. His results were "immediately gratifying" but the number of cases was not given.

Scott and Schroeder in 1938 again emphasized the necessity for transecting the lateral sympathetic chains as well as the presacral nerve if the objective is to do away with painful sensations from the fundus of the bladder. Pain and bladder spasm produced by inflammation of the trigone and bladder neck, as occur in vesical tuberculosis, can be relieved by presacral neurectomy alone, but relief of the symptoms of interstitial cystitis usually requires interruption of the lateral sympathetic chains also. The authors report their results in 11 cases, 8 of which had tuberculous cystitis and three had interstitial cystitis. Of these 3, one was greatly improved for at least 1 year, 1 relapsed in 6 months perhaps because of a marked urinary infection, and in one the symptoms were improved but not entirely relieved.

Both Pieri and Band are of the opinion that in order to interrupt completely the afferent pathways from the bladder, both presacral neurectomy and section of the sympathetic chains at the level of the sacral promontory are necessary.

Much of our knowledge of the neurology of the bladder is due to the researches of the French school. Jaboulay (quoted by Learmonth) in 1899 suggested interruption of the vesical nerves in the treatment of bladder pain. Latarjet, Richer, Rochet and Cotte have published the results of their study of pelvic nerves. French urologists, and Spanish urologists as well, have been more interested than we in utilizing the knowledge gained from the researches just mentioned. Victor Richer, in 1939, published a paper on the section of the erector nerves of Eckardt, combined with section of the hypogastric nerves, in patients with rebellious cystitis. Darget and Chemilleau and Serrallach Juha have described methods of injecting novocaine into the region of the hypogastric plexuses through a parasacral approach.

Urologists should be aware of the part which neurosurgery can play in the relief of vesical pain, but in a quite inadequate review of this phase of the treatment of interstitial cystitis, I have not found much evidence of clinical benefits. David Band, in a recent summary of the role of neurosurgery in the treatment of vesical pain says: "In the relief of cystalgia neurosurgical intervention from the level of the spinal center in the conus medullaris downwards would appear to be inadequate unless the motor innervation of the bladder is to be sacrificed."

doubtful that they obtain even palliative improvement. We shall continue to use radiocobalt therapy in these two types of lesions in an effort to improve the radiation dosage and so gain more experience as to the limitations of this method of radiation therapy. Experience so far indicates that the method will be of some avail in a limited group of lesions only. A combination of intracavitary radiocobalt therapy with external x-ray therapy to the paravesical tissues is under consideration at present. Such a method would have much in common with the well known and effective treatment of cancer of the uterine cervix with radium and x-ray.

The increase in capacity may be due to the absence of pain when the bladder is distended. According to this theory there would be no need for overdistention, yet in some cases repeated and less forcible distention will result in marked improvement. The explanation of the improvement may be that the filling of the bladder several times at each visit acts as massage on the area of lymphatic stasis and stimulates the circulation locally, or that improvement in the local circulation, by reducing edema and leukocytic infiltration, decreases the abnormal sensitivity of the nerves involved.

Other types of local treatment have been tried. Among these are the injection of absolute alcohol into the diseased area with the purpose of destroying the nerves contained therein (Alexander). A method which has been widely used has been the instillation into the bladder of silver nitrate solution in gradually increasing strength until a solution of 1 per cent or of even greater strength has been reached.

Local treatment based upon an entirely different philosophy has consisted of the instillation of soothing oils—mineral oil, cod-liver oil, gomenol, cajandol and undoubtedly many others.

Radiation of the bladder by the roentgen ray and the application of short wave diathermy have been employed.

Overdistention of the bladder together with fulguration of the areas of redness, especially those which crack and bleed as a result of dilatation, are the most commonly accepted measures employed in interstitial cystitis. Resection of the area of fibrosis would seem to be the most logical method of treatment if it were not for the likelihood that other areas will develop secondarily.

Systemic Methods of Treatment

Attack has been made upon the local lesion by means of substances introduced into the general circulation. Solutions of peptone and of neo-arsphenamine have been given intravenously, potassium iodide, alpha-tocopherol, ipecac and estrogens orally. The sulfonamides have of course been tried as has streptomycin. With all these therapeutic measures, some patients were relieved, temporarily, enough to inspire some urologist to publish the reports of a few patients whose improvement he attributed to this new method. Antibacterial drugs would seem a priori to have little value. The use of drugs such as potassium iodide or possibly cortisone which tend to soften fibrous tissue seems logical.

My experience with interstitial cystitis includes about one hundred patients seen between the years 1914 and 1951. A number of these patients were seen only once or twice, the diagnosis was made but the patients failed to come back for treatment. There were 49 women and 15 men who did return for treatment for a sufficient period of time to enable me to draw some conclusions as to the effectiveness of the measures employed.

The 49 women in this group fall into four classes as follows:

Group 1 Apparently cured, 13 cases. The criteria for including patients in this group are a) freedom from pain which could be caused by the bladder condition, b) ability to hold urine for at least 2 hours, c) a duration of these two criteria for

(minor sciatic notch) by Cunningham, Morris, Gray, Braus, Sobotta, Toldt, and only Coining indicates in his drawing a high division at that point

REVIEW OF LITERATURE

Pudendal neurectomies were reported by Rochet in 1899, 1903, and 1921, Tavel in 1902, Albertin in 1903, Michon and Wertheimer in 1923 and 1928, Huggins, Walker and Noonan in 1939, Emmett, Daut and Dunn in 1948, and Nesbit in 1948. The following conditions are listed as indications: cystalgia and urinary

TABLE 1 *Ramification of Pudendal nerve (After Tavel)*

<i>Normal Innervation</i>		<i>Important Innervation</i>
Inferior Hemorrhoid N	{ Post half of anal sphincter Post part of peri-anal skin	{ Inferior Hemorrhoid N
Superficial Perineal N	{ Ant part of the perianal skin Perineal skin Post part of skin labia majora scrotum	{ Superficial Perineal N
Deep Perineal N	{ Ant half of anal sphincter Superficial transverse perineal m Ischio cavernosus m Bulbocavernosus m + constrictor cuni Post part deep transverse perineal m Post part of labia minora Post part of vulva (hymen)	{ Deep Perineal N
	{ Vaginal mucosa Urethral mucosa Striated vaginal muscles Striated urethral muscles Ant part of deep transverse perineal m Ant part labia minora Ant part of vulva (hymen)	
Dorsal Penis (clitoris) N	{ Corpora cavernosa (penis—clitoris) Glans (penis—clitoris) Skin (penis—clitoris) Prepuce (penis—clitoris)	{ Dorsal Penis (clitoris) N

reflex retention due to pain, vaginismus and pruritus, kraurosis vulvae and pain from a vulvovaginal epithelioma, nontraumatic neurogenic bladders, traumatic cord bladder. Huggins, Walker and Noonan observed five good results among seven tabetics (in conjunction with presacral neurectomy and transurethral resection). Emmett, Daut and Dunn failed in 1 case to restore the function of a traumatic cord bladder, possibly due to incomplete neurectomy, and Nesbit achieved a good result in 1 case of traumatic cord bladder.

Pudendal nerve blocks with an anesthetic agent were reported to have a temporary effect in tabetic bladders. In 1945 we presented the first permanent result with this method and succeeded in restoring a balanced function to a traumatic

carried out in some patients in whom it was not done. Those who did best were the patients in whom the fulguration was the most thorough. Of the 13 cases in the 'cured' group, only one had no fulguration, she was treated by bladder dilatation with dilute silver nitrate solution. One was cured by resection of the area of fibrosis and remained well for at least 6 years. In another the best response followed two injections of absolute alcohol into the ulcer. She was well $2\frac{1}{2}$ years later.

A patient in whom subtotal cystectomy was done grew a new bladder fundus with a capacity of 240 cc. Seven years after the bladder resection she developed several areas of typical interstitial cystitis. These were fulgurated and she is now quite free from pain.

Ureterosigmoidostomy was done in one of the patients who was not helped by 3 years' treatment of the bladder. This patient died a few months later, probably of carcinoma of the liver.

In 40 per cent of the women, granular urethritis was present as well as a definite interstitial cystitis. The urethritis was diagnosed by endoscopy and was

TABLE 1 *Age at which symptoms began in men*

AGE	NUMBER
30-39	4
40-49	4
50-59	2
60-69	5
Total	15

treated by cauterization, light fulguration and dilatation of the urethra. Pain during urination is strongly suggestive of urethral involvement, it is not due to interstitial cystitis.

In the group of men with interstitial cystitis, there were 15 whose records are sufficiently complete to be of some value. The age at which symptoms first began to trouble these was somewhat greater than in the group of women (table 1).

The symptoms also were somewhat different. There was not the acute pain in the bladder, often localized in the suprapubic area, which was so frequently a cause of complaint in women. Pain in the men occurred only when the bladder was overdistended, the chief complaint was of frequent urination and an overwhelming desire to void when the bladder was filled to its capacity. Three had had transurethral resections of the bladder neck without relief through failure of the urologist to recognize the true cause of the patient's frequency.

Four showed evidence of infection in the urine, either by the presence of pus or by a positive culture. Eight showed neither of these findings. In 3, the presence or absence of infection was not definitely determined. Only 2 had residual urine, one 45 cc, the other 60.

The diagnosis in all cases was made by cystoscopy. In 7 there was a definite Hunner ulcer, another patient showed a ridge of scar indicating a preceding lesion.

RESULTS

An undivided solid trunk of the pudendal nerve was found only once unilaterally, while a division into two branches was encountered nine times (four times bilaterally and once unilaterally). Three branches were observed twice, (bilaterally in the same patient). The medial branches were larger than the lateral and when three branches were present the medial and intermediate were almost equal in size, but thicker than the lateral.

The bladder function of all patients became well balanced postoperatively, i.e. the relationship of $\frac{\text{Residual}}{\text{Capacity}}$ was below 20 per cent, calculated on a minimum

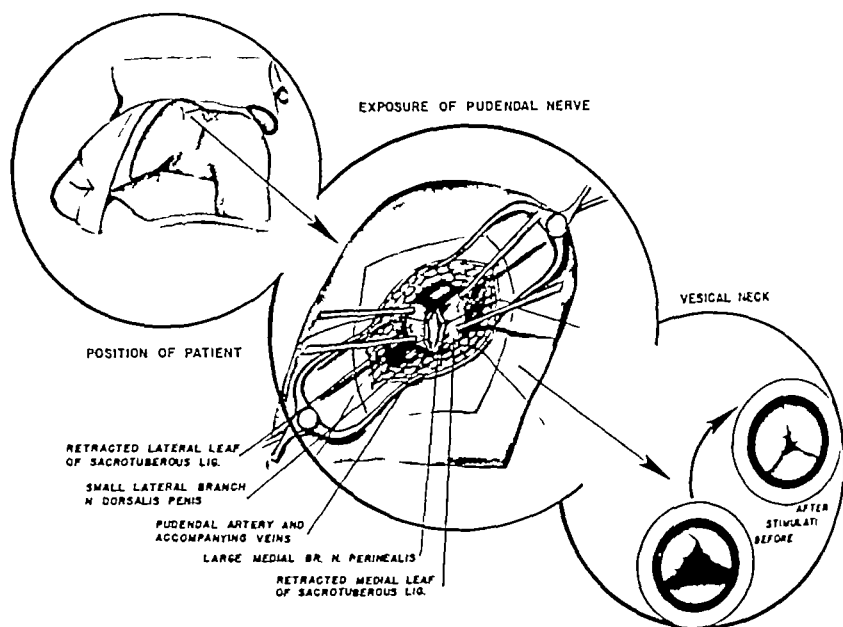


FIG 1

capacity of 300 cc which is compatible with an upper motor neuron lesion. However, one patient whose bladder neck was repeatedly resected, was improved, although his residual occasionally exceeded 20 per cent. This, most likely, was connected with the patient's general morbidity and depressive mental condition. Table 2 illustrates detailed clinical and physiologic observations following bilateral pudendal neurectomy. In only 1 case did the patient's vesical neck remain closed after bilateral pudendal neurectomy, despite a preceding transurethral resection. That same patient did not lose erections postoperatively. It is possible that fibers were spared inadvertently, inasmuch as this was only the second case of the series and no stimulation was done at that time. There was no incontinence, an observation known to earlier investigators.

The responses to electric stimulation of the intact and severed nerves in com-

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With one exception the brisk response occurred on stimulating the distal stump of the medial branch. In this exceptional case it occurred on stimulating the lateral branch.

TABLE 3 *Summary of response to stimulation of 7 pudendal nerves on 4 patients*

	PELVIC FLOOR	VESICAL NECK	MAS. REFLEX
Nerves Intact			
Solid Trunk (1)	+(1)	+(1)	+(1)
Medial Branch (7)	+(7)	+(5) ?(2)	-(2) ?(1)
Lateral Branch (5)	+(4)	+(3) ?(1)	+(1) ?(1)
Intermediate Branch (2)	+(2)	+(2)	+(1)
Proximal Stump			
Solid Trunk (1)	+(1)	?(1)	+(1)
Medial Branch (5)	+(2)	+(1) ?(1)	+(3)
Lateral Branch (2)	+(1)	?(1)	+(2)
Intermediate Branch (1)	—	—	+(1)
Distal Stump			
Solid Trunk (1)	?(1)	+(1)	—
Medial Branch (6)	+(3) ?(1)	+(5)	—
Lateral Branch (4)	+(1)	+(1)	—
Intermediate Branch (2)	—	+(1)	—

DISCUSSION

Although this study is based on a small series of cases it revealed a number of interesting observations.

The very weak response of the pelvic floor to stimulation of the distal stump as compared with the strong contraction by stimulation of the intact nerve or proximal stump suggests that those authors are correct who deny that the pudendal nerves innervate the levator ani.

Tavel's anomaly was found in one instance in which stimulation of the lateral branch (dorsal penis nerve) produced a contraction of the vesical neck indicating that it supplied the periurethral striated muscles also.

In all, except one, of the twelve dissections, the pudendal nerve divided underneath the sacrotuberous ligament. Usually two branches (medial perineal nerve, lateral dorsalis penis nerve) were found at this point, contrary to most text books which describe a more distal division in Alcock's canal.

A contraction of the vesical neck occurred 5 times in 6 instances on stimulation of the distal stump of the medial branch. It is believed that this failure could have been omitted if more than 1 volt had been applied. After removal of the cystoscope 3 volts were applied in the same case and this resulted in retraction

RATIONALE OF TECHNIQUE

The rationale for this method of radiation therapy is based on the dose distribution from a centrally located "point source" of radiation. Two factors are here involved: a) inverse square law which governs the distribution of radiation,

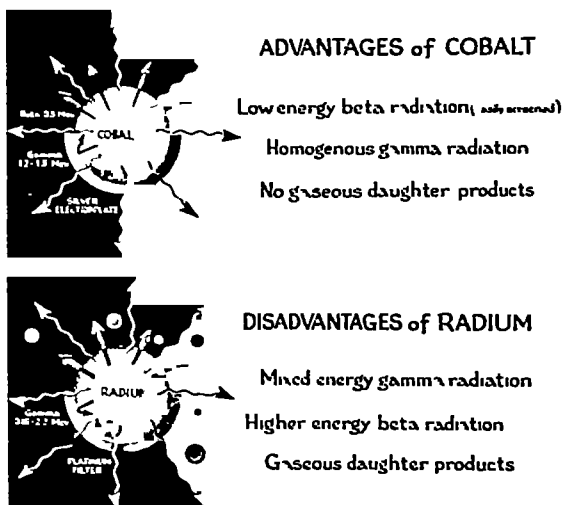


FIG 1 Advantages of radiocobalt over radium

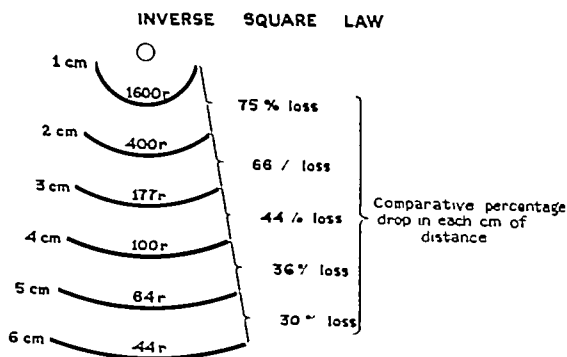


FIG 2 Example of application of inverse square law

b) absorption of radiation which determines the dose when a gamma ray emitter radioactive substance is used as a "point source" for intracavitary radiation:

Intensity of radiation decreases inversely as the square of the distance. When a radioactive substance is in contact with a tumor three fourths of the intensity at 1 cm tumor depth is lost at 2 cm depth per unit area. If the source is separated 3 cm from the tumor surface, the loss at 2 cm depth is then less than one-third of that at 1 cm tumor depth (fig 2). Consequently, with increased distance

* Friedman M and Lewis L G Radiol 53 342-361 1949

anesthesia is an indirect method of demonstrating a relationship between pudendal nerves and bladder neck. It occurred in 53 per cent of the first 56 cases and in 36 per cent of the additional 39 patients. It is less constant and far less convincing than the direct method of stimulation. A combination of presacral and bilateral pudendal neurectomy seems not advisable because it would lead to complete paralysis of the vesical and urethral sphincters. The calibrated method of weakening the vesical sphincter by transurethral resection in combination with pudendal block or neurectomy is less hazardous to urinary continence.

The dual innervation of the vesical neck seems to be significant for the concept of the physiology of micturition. While it proves that electrical stimulation of the pudendal nerve leads to contraction of the vesical neck in addition to the contraction of the external urethral sphincter, it appears not unreasonable that a similar process takes place on volitional contraction of the external urethral sphincter. Conversely, one would expect that relaxation of both sphincters could be induced as a direct mechanism despite reports to the contrary. Thus the presented data would support the statement of those who claim that "micturition on volition" can be induced at will through volitional relaxation of the sphincters with an associated contraction of the detrusor.

The following pathophysiologic and therapeutic considerations can be better understood also in the light of the dual innervation of the vesical neck. Neurogenic dysfunction of the bladder cannot be blamed any longer exclusively on the detrusor, i.e. on the smooth muscles of expulsion, but also on the smooth and striated forces of retention, including the somatically innervated pelvic floor. If efficient reflex micturition is integrated on a spinal level in upper motor neuron lesions, it implies that coordination is present between the contraction of forces of expulsion and reciprocal relaxation of forces of resistance, including the striated muscles of the pelvic floor. In mild degrees of disturbance of reciprocal relaxation paradoxical inhibition is not infrequently observed, i.e., a voluntary strain of the patient during voiding touches off a spinal mass reflex which spreads also to the pelvic floor due to the loss of its reciprocal inhibition. The contraction of the striated urethral sphincter leads to a reflex relaxation of the detrusor and the entire mechanism can be used by the patient for a volitional interruption of the urinary stream. This degree of incoordination is initiated at will, it is reversible and temporary because it ceases with the discontinuation of the wilfully induced mass reflex, the next degree of incoordination, that of permanent loss of reciprocal innervation results in more or less complete retention but it can be treated successfully, even after years, by procedures directed at the pudendal nerves. The recognition of this condition should help to reduce the number of reported failures of transurethral resection. In these cases the calibrated tenotomy of the vesical neck by transurethral resection followed by pudendal intracane blocks or neurectomy appears to be a promising combination when any single of the methods may fail to yield the desired result.

SUMMARY

Bilateral pudendal neurectomies were done on 6 patients with a neurogenic dysfunction of the bladder subsequent to upper motor neuron lesions, five were

The balloon is filled with 50 cc of a mixture of dilute solution of cobalt to which 1-2 drops of methylene blue has been

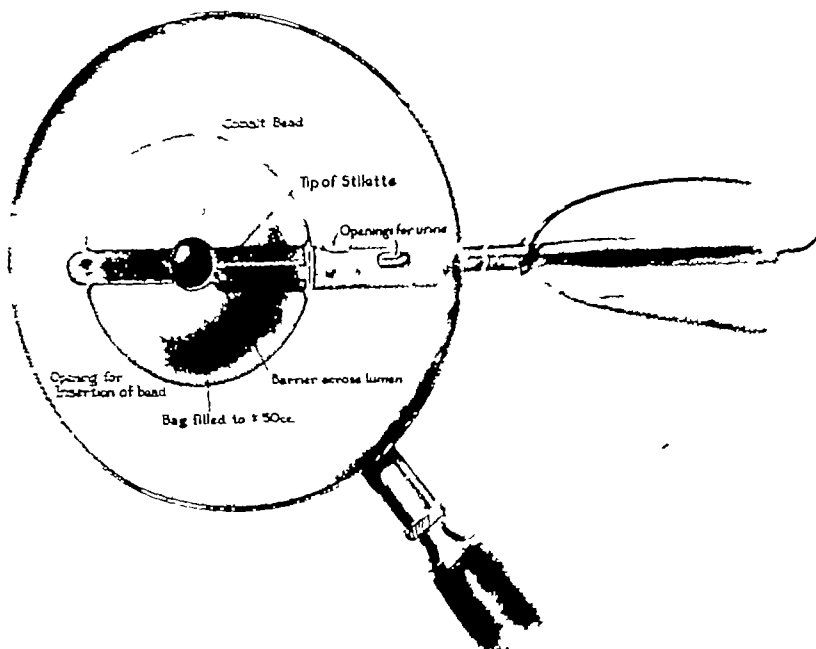


FIG 4 Modified balloon catheter for radiocobalt administration, cystostomy



FIG 5 AP roentgenogram with iodide filled balloon, added AP, lateral, and oblique roentgenograms are made, distance from bead to tumor, and, second, to urethra (fig 5)

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with edema and intense erythema, which takes about two months to subside, leaving a bladder of smaller capacity

TABLE 2

PT.	AGE	SEX	TYPE OF TUMOR	FOLLOW UP	REMARKS
<i>Infiltrative tumors</i>					
R C	78	F	Papillary carcinoma "Grade III"	Too recent to determine result	Previous deep x-ray therapy elsewhere
C S	75	F	Transitional carcinoma	cell	No improvement Dying of carcinomatosis
E R	58	F	Transitional carcinoma	cell	Developed "pyo bladder" 1 month later Right ureteral transplantation
M H	64	M	"Anaplastic" carcinoma	No Improvement	Bladder tumor extended in spite of bilateral ureteral transplantation and deep x-ray therapy
C M	56	M	"Anaplastic" carcinoma	Recent case No apparent improvement	Ureteral transplantation
F S	66	F	Anaplastic" carcinoma	No improvement	Ureteral transplantation. Died in 2 months of carcinomatosis



FIG. 6 A M (female aged 66) A, multiple benign papillomas, with two exposures to cobalt 3 months apart B 5 months after initial treatment Well 2 years later except for small bladder capacity (Subsequently developed recurrence)

RESULTS OF THERAPY

Papillomatosis and localized tumors responded more often (table 1) than infiltrative tumors (table 2) in which even palpation was not seen. Of the 13 patients followed long enough for evaluation of immediate results, 6 received some benefit but among these, only one has remained free of recurrence. We can draw no conclusions, however, from such a small series and so short a follow-up

VESICOVAGINAL FISTULA, A SIMPLIFIED METHOD OF REPAIR

LLOYD R. REYNOLDS, T. L. SCHULTE AND HOWARD J. HAMMER

Few lesions that confront the urologic surgeon present a greater challenge than that encountered in the repair of vesicovaginal fistulas. An almost endless review of surprisingly varied surgical approaches, principles of preoperative and postoperative care and other dogma have appeared in medical literature for the past two centuries. The wide divergence in opinion clearly indicates that the incidence of failures has been too great. Miller, who has presented an outstanding contribution, reviews history, techniques, and statistics relative to vesicovaginal fistula.

Among others, Counseller has described reasons for failures. Inadequate exposure from various positions, failure to excise all scar tissue, suturing into the vesical mucosa, superimposition of suture lines and faulty postoperative management are stressed as factors that result in poor surgical results. Mobilization of the bladder and excision of the fistulous tract are emphasized as important adjuncts to the surgical management.

It is our purpose to present a method of repair that simplifies and circumvents many problems ordinarily encountered in the surgical treatment of this condition. We are in accord with those who point out that the vaginal approach is not only the most popular, but the best. Urologists have increasingly been called upon to assist or completely consummate both diagnostic and surgical treatment of this condition. Many urologists prefer the suprapubic or transvesical approach.

About 20 years ago, the late Dr. A. V. Pettit of the Stanford gynecological service and one of us (L. R. R.) collaborated in developing this method of repair. In 1943 Dr. Pettit reported 15 cases which had been successfully repaired. While the principle involved has been used in surgery of other structures, we believe that its development in the surgical repair of vesicovaginal fistula to be original with us.

We refer to the method as a "patch" repair of the defect because there is no suturing of the bladder mucosa attempted. The defect is covered with a "patch" or flap of vaginal mucosa. The original procedure has been slightly modified in the past few years and in our hands has produced cures among patients with single and multiple fistulas, many of whom had been subjected to previous surgery.

TECHNIQUE

Preliminary urologic evaluation is carried out in all cases. Although localization of the fistulous tract is carefully ascertained, the method to be described may be applied to metervaginal or urethrovaginal fistulas as well as to the repair of defects situated above the vesical trigone. Vaginal hygiene and treatment of urinary tract infection are preoperative considerations. Too early operation is to be avoided.

Read at annual meeting, Western Section, American Urological Association, Sun Valley, Idaho, June 27, 1951.

without evidence of recurrence. However, after about 14 months she was cystoscoped and found to have a fairly large new papilloma surrounded by myriads of small seedlings on the posterior bladder wall (fig 7, A). A biopsy again showed malignant papilloma, and she was given a total of 6200 roentgens radiation with radiocobalt at one treatment. After 6 weeks, although she still had a rather severe radiation cystitis, the papillomas had disappeared. At 3 months, her bladder mucosa appeared normal, and no evidence of papillomas could be seen (fig 7, B). She is still being observed at 3 month intervals and so far has had no recurrence.

3 Infiltrative tumor. Mr M. H., aged 64, was found to have anaplastic infiltrating carcinoma (fig 8, A). He was given radiocobalt therapy, bilateral ureteral transplantation and deep x-ray therapy without significant effect, either curative or palliative (fig 8, B).

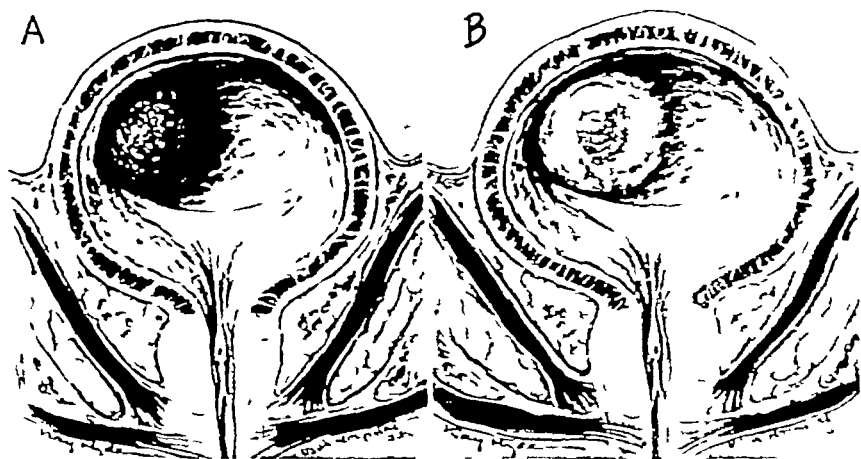


FIG 8 Infiltrating tumor M. H. (male, aged 64). A anaplastic infiltrating carcinoma treated with radioactive cobalt, bilateral ureteral transplantation and deep x-ray therapy. B, poor final result 4 months later.

DISCUSSION

We had hoped that this new modality of radiation therapy would help us in the treatment of the two groups of patients who are least satisfactorily treated by present methods. The first, multiple papillomas, are very hard to treat by resection or fulguration and are not considered sufficiently malignant in potentiality to warrant radical cystectomy and ureteral transplantation with its attendant discomfort and morbidity. The second, infiltrative lesions which are into or through the muscle, are beyond cure by resection or radical operation. The lesions between these extremes are best treated in our hands by thorough transurethral resection or by cystectomy, without radiation therapy.

Our experience, while limited, leads us to feel that multiple papillomas may respond to intracavitary radiation, but if not surgical treatment, including cystectomy if necessary, should be used. Advanced, infiltrative lesions, at the other extreme have received no curative benefit, and it has become increasingly

the bladder wall is not used in the closure the vesical capacity is not further contracted, which is an important consideration in dealing with large or multiple fistulas

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EFFECT OF ELECTRIC STIMULATION OF THE PUDENDAL NERVES ON THE VESICAL NECK, ITS SIGNIFICANCE FOR THE FUNCTION OF CORD BLADDERS A PRELIMINARY REPORT

ERNEST BORS

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Previous publications dealt with the beneficial results of bilateral pudendal nerve anesthesia for the restoration of a balanced function of traumatic cord bladders. Additional, as yet unpublished, data of a large series of patients confirmed earlier physiologic observations of a relationship between the pudendal nerves and the vesical neck visualized cystographically while the pudendal intracane block lasted. It was, therefore, a logical development to observe the vesical neck cystoscopically and its response to electric stimulation of the pudendal nerves exposed at operation of such patients in which a pudendal neurectomy was indicated. This indication arose when the bladder function failed to benefit permanently from pudendal anesthesia, but responded favorably, though temporarily, to each of a series of at least six pudendal intracane blocks. It appears worth while to report the results of six bilateral pudendal neurectomies and of electric stimulation of seven pudendal nerves on 4 patients.

ANATOMICAL REVIEW

The derivation and gross anatomy of the pudendal nerve have been well described or illustrated. The review of the literature is, therefore, confined to the following three pertinent problems: 1) Which nerves carry the motor supply to the levator ani? There is lack of agreement among the authors. Cunningham, Morris, and Cornung ascribe this function to the deep perineal branch of the pudendal nerve. Moeller and Mueller, Toldt, Sobotta and Tavel state that the pudendal and coccygeal plexus but not the pudendal nerve carry motor fibers to the levator muscle. A compromise solution is offered by Gray and Braus. According to these investigators the levator ani receives its motor supply from the pudendal plexus via S-3, S-4 and from the coccygeal plexus, but that occasionally additional fibers derive from the perineal or inferior hemorrhoidal nerves. 2) What important anomaly is encountered in the innervation of the striated perineurethral muscles? Tavel states that the dorsalis penis nerve supplies these structures not infrequently, instead of the normal innervation by the deep perineal branch of the pudendal nerve (table 1). 3) At which anatomical landmark does the pudendal nerve divide into the perineal and the dorsalis penis nerves? The nerve is described as a solid trunk underneath the sacrotuberous ligament.

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stilled, the catheter was then clamped during 24 hours. The volume, specific gravity and the amounts of urea and chlorides, recovered in the urine 24 hours later by opening the catheter, were considerably lower than those observed the previous day. Therefore he concluded that water, urea and chlorides are readily absorbed from the normal bladder of mammals.

2 *Absorption of exogenous substances* Regarding the resorption of exogenous compounds from the urinary bladder there are 3 main features which seem to influence its magnitude and speed:

- 1) The molecular size of the substance
- 2) The concentration of the solution
- 3) The status of the epithelium

The first point has been clearly demonstrated by Streller and Vondra and still better by Schän. They show that substances in ionic dispersion have a higher absorption ratio than molecules and the latter a higher ratio than colloids. Therefore dissociable substances like inorganic salts are the most readily absorbable while proteins and lipids which usually occur in colloidal states have the lowest ratio of absorption.

An exception to this rule is the one regarding substances with high antigenic activity. It has been reported by Baretz, Harten and Walzer that the sensitization of cutaneous areas of the rhesus monkey with 0.05 ml. of serum from a patient who was highly sensitive to cottonseed followed by the intravesical instillation of cottonseed oil was followed 7 or 8 minutes later by marked wheal formation in the sensitized areas. This work was offered as corroboration of the previous reports of Remling and Bailly regarding absorption of the rabies virus from the bladder, also for Akaeda's work on sensitization by intravesical instillation of various animal sera or erythrocytes. Therefore antigens may be absorbed from the bladder in spite of their high molecular weight.

The difference in the absorption ratio of a solution seems also to be influenced by its concentration. Therefore as in any dialysis experiment hypertonic solutions are more readily absorbed than iso- or hypotonic solutions. The following experiment of Schar proves this point categorically.

Solutions of different concentrations of sodium iodide were instilled into the bladder of the dog which had been excluded from the upper urinary tract by ureteral anastomosis to the skin. The solutions were left 30 minutes in contact with the mucosa. After this interval the bladder was evacuated and rinsed several times with distilled water. The sodium iodide which had been determined previously by titration was now measured in the amount recovered from the original solution and in the rinsing water. The difference was considered as absorbed. Results were as follows:

CONCENTRATION OF SOLUTION	RATIO OF ABSORPTION IN %
1%	25.0
2%	33.3
5%	40.3

cord bladder The method was originally intended to differentiate structural from functional changes of the vesical neck in order to select the proper type of therapy After a comprehensive study of the physiological observations connected with the procedure in 1948, the method has been used as well for therapeutic purposes In 1948 Emmett, Daut and Dunn reported their experience with this procedure in a limited number of patients with normal bladders and traumatic cord bladders with but temporary restoration of bladder function in the latter group

CLINICAL DATA

Selection of patients Five patients had cord bladders as the result of injury and one subsequent to an epidural abscess All had cord lesions of the upper motor neuron type After routine management, including tidal drainage and bladder training, they were all subjected to a series of pudendal intracaine blocks with complete examinations of the bladder before and after anesthesia as outlined previously and all had unsatisfactory bladder function Their conus proved to be active on testing the bulbocavernosus and anal reflexes and rectal sphincter tone They all responded well immediately to the pudendal nerve block, but the improvement was only temporary Their age ranged from 25 to 38 years Their cord lesions were clinically complete at levels between D-5 and D-12 Two cases underwent transurethral resections of the internal vesical orifices before the pudendal neurectomy One patient was resected twice, 33 and 35 months after injury, the other only once, 12 months after injury In the first case, a total of 22 gm was removed, in the second 8 gm The bilateral pudendal neurectomy was made in two stages three weeks apart Operation was performed from 1 to 5 years after injury

Operative procedure A modified approach of Huggins, Walker and Noonan was chosen (fig 1) A 24F panendoscope was introduced under vision and the response of the vesical neck to electric stimulation a) of each of the intact nerves, b) of the proximal segments of each severed nerve and c) of the distal portion of each severed nerve was observed After completion of this part of the intervention and with the nerves cut, the patient was returned to the abdominal position and the wound repaired

In two instances the Lovett-Garceau stimulator was used, while in the remaining five examinations the Hinsey Geohegan instrument was employed The stimulus applied was a 60 cycle sine wave at 1.6 rms volts, measured under load In all cases, except one, a stimulus of 1 volt applied for one second sufficed to elicit a response In this case 3 volts for one second were needed Before each stimulation the bipolar electrodes were tested on the exposed fibers of the gluteus muscle The observer remained uninformed of the structure stimulated by the operator

Sphincterometrograms and cystograms were done prior to the unilateral neurectomy, immediately after the unilateral neurectomy, the day before the bilateral neurectomy, and eventually, after bilateral neurectomy The same study was carried on as a follow-up at longer intervals

By a keenly planned experiment carried out by Schär, the route followed by the absorbed substances has been demonstrated. He instilled India ink into a dog's bladder which had been surgically excluded from continuity with the upper urinary tract and sacrificed the animal 24 hours later. He eliminated heme pigments as a source of error by immersion in a diluted ammonia solution and then rinsed the tissues until staining tests for iron were negative. In multiple sections the India ink particles were found in the perivascular spaces as well as in the lymphatic spaces. The particles were also found to have been phagocytosed and transported by histiocytes and to have been included in the endothelial cells of the capillaries' walls. Detection of India ink at the regional lymph nodes and even from the spleen was noticed. By producing vasoconstriction with adrenalin Schar further proved that under vasospastic conditions most of the absorbed substances were found in the lymphatic spaces but concluded that both systems were effective routes of absorption from the urinary bladder.

II. TRANSFORMATIONS OF TRANSITIONAL EPITHELIUM BY HORMONES

Epithelial cells have a potentiality for adaptation to normal and pathological stimuli. This has been repeatedly demonstrated in the pathology of malignant epithelial neoplasms and by the experimental influences upon normal epithelial layers.

It is known that the epithelial layer which lines the bladder is not a mucosa in true secretory meaning of the word. With the exception of the trigone in which Albarran and others have demonstrated the presence of glandular elements, the lining of the bladder does not possess glandular structures.

At the trigone two sorts of glandular formations have been described, some, of a cylindrical or racemous shape, are epithelial depressions lined with the same transitional epithelium as the rest of the organ and the other sort consists of small depressions lined by a single layer of prismatic cells. These latter structures seem to secrete a similar material to the one produced by the urethral glandular formations and to react in identical form to stimulation with estrogens. Huggins has described the squamous metaplasia noticed in the epithelium of the posterior urethra under the influence of estrogens and the same holds true for these structures as has been shown by extensive studies of Cifuentes Delatte. This area of the trigone has furthermore been described to possess a cyclical exfoliation similar to that which occurs in the vagina, it is present exclusively in females. This finding has led del Castillo, Argony and Maimmi to its clinical use for evaluation of estrogen activity in the normal human female.

Working also with estrogens Lacassagne noticed intense proliferation of the epithelium of the dome of the bladder with the presence of true neoplastic features as mitosis and anaplasia. The polyhedral cells described by him grew toward the lumen of the bladder as well as toward the submucosa. Murray and Steinkamm tried to corroborate the results of the Paris laboratory without success but noticed that prepuberal castration produces a great diminution in the size and thickness of the bladder, all layers included. Their work was performed on albino rats.

piled in table 3 according to contraction and elevation of the pelvic floor, contraction of the vesical neck and mass reflex. Stimulation of intact nerves could obviously cause conduction in two directions, namely caudad and cephalad. It is, therefore, not surprising that mass reflexes appeared, precipitated either directly by afferent fibers or by antidromic conduction. The response of the pelvic floor was always stronger and more constant than that of the vesical neck. When mass reflexes appeared they spread quickly, cephalad and caudad, to abdomen and both lower extremities respectively.

TABLE 2 *Physiologic and clinical observations 6 cases*

	BEFORE			AFTER		
<i>Sphincterometry</i>	Well above normal* 52-146 mm Hg			Within normal limits 14-30 mm Hg		
	Open	Closed		Open	Closed	
<i>Vesical Neck</i>	3 (1 TUR)†	3 (1 TUR)		5 (1 TUR)	1 (1 TUR)	
<i>Capacity</i>	Essentially Unchanged					
	High	None		Low	None	
<i>Residual</i>	5 (120-300 cc)	1		5 (15-30 cc)	1	
	Effective	Ineffective		Effective	Ineffective	
<i>Extrinsic Pressure (Strain—Crede)</i>	0	6		6	0	
	Complete	Partial	Absent	Complete	Partial	Absent
<i>Erection</i>	3	2	1	1	1	4
<i>Stress Incontinence</i>	None			None		

* Normal—20-40 mm Hg

† TUR—Transurethral Resection of Vesical Neck

Stimulation of the proximal stump of the severed nerves precipitated, with two exceptions, mass reflexes. However, the response of the pelvic floor was less frequent and that of the vesical neck occurred only once. This response will be discussed later.

Stimulation of the distal stump of the severed nerves was conspicuous by a complete absence of mass reflexes and by a much weaker contraction of the pelvic floor than when the intact nerves or the proximal stump were stimulated. Conversely, there was a distinct and strong, almost isolated, contraction of the vesical neck. It started as a brisk movement that slowed down gradually as it approached the condition of complete closure. This was quite different from the weak and fleeting movement precipitated by stimulation of the intact nerves.

These data though suggestive have been obtained by artificial means and are not the product of the normal, intact vesical epithelium. Therefore it was our aim to use an experiment in which no foreign solutions were introduced and in which no possibility of trauma or manipulation of the mucosa could invalidate the results.

V TECHNIQUE OF VESICAL ISOLATION

In order to study these physiological phenomena we considered the isolated bladder (fig 1) as the ideal organ for study. By that it is implied that the organ possessed a complete and intact blood, lymph and nervous supply but without continuity with the upper and lower urinary tract. This was accomplished by surgical performance of a bilateral ureterosigmoidostomy to the distal large bowel which had been previously excluded from the fecal stream by a preliminary colostomy and by the section and ligation of the vesical neck. Ureterosigmoidostomy into the intact bowel is known to carry a high morbidity among dogs

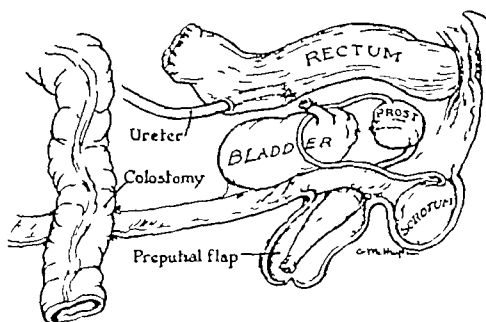


FIG 1 Diagram of vesical isolation used in present experiments

and therefore the large bowel was first excluded from its usual fecal passage, and antibiotic therapy was used.

This experiment was performed on 9 healthy male dogs of medium or large size (with body weights varying between 15 and 25 kg). The dogs were observed for several days before being selected for the experiment to rule out the possibility of either urologic or general disease that might have influenced the validity of the results. Weekly control of the weights was recorded during the time of the experiment to assure the conservation of their health, and changes in their ingestion and excreta were recorded.

Colostomy. About half an hour before operation, morphine sulfate 15 mg and atropine sulfate 0.6 mg were injected subcutaneously. The colon was then irrigated with tap water until the return fluid was clear.

Under ether anesthesia the peritoneal cavity was entered through a left rectus incision, the middle of which was at the level of the umbilicus. The descending colon was delivered through the incision and the bloody supply of a segment was ligated over a distance of about 15 cm. The colon was doubly ligated with silk and transected. A catgut purse-string suture was then placed in the distal colon about 6 cm beyond the transection and the ligated distal end invaginated, several interrupted sutures were then placed in the muscularis of the distal

of the penis, characteristic for the contraction of the bulbo- and ischioavernosus muscles, from cystoscopic observation on other cases this was known to occur with a simultaneous contraction of the vesical neck

The contraction of the vesical neck with stimulation of the proximal stump of the medial branch appears to be a part of the mass reflex initiated by stimulation of sensory components of the pudendal nerve and activated by discharges through the efferent fibers of the presacral nerve

The findings imply that the vesical neck has a dual innervation 1) from the presacral nerve and 2) from the pudendal nerve Based upon the myological studies of McCrea, the striated peri-urethral musculature, part of which forms the urethral sphincter, extends farther up and is connected with another, so-called 'external vesical' sphincter, which lies just distally to the smooth "internal vesical" sphincter Rochet, Young and Wesson, and McMahon have mentioned an extension of the striated muscles of the urethral sphincter to and past the vesical neck and into the trigone This intertwining of striated and smooth musculature is the result of an early embryological development in the cloacal region The cloacal sphincter is originally a skeletal striated muscle which arose independently from the tail muscles A remnant of the tail muscles in man is the pubococcygeal muscle which, as levator ani and the much less developed coccygeus muscle, helps in forming the pelvic floor In primates these muscles are said to mix with, and become closely related to, the cloacal (striated) muscles and, by intertwining fibers to the visceral (smooth muscles) This does not occur in predatory animals where the striated ileo-pubo-ischio-caudal group remains completely separated from the cloacal muscles and therefore from the viscus This anatomical difference, among others, makes experimental findings in cats not translatable to man Where the presacral innervation ends and the pudendal innervation starts remains unknown Interruption of either nerve makes a cord bladder amenable to extrinsic pressure Conversely stimulation of the presacral or pudendal nerve initiates a contraction of the vesical neck However, it is probable that presacral nerve stimulation produces primarily a contraction of the smooth muscle component of the bladder neck, while pudendal nerve stimulation activates primarily the urethral sphincter and the striated muscle components of the bladder neck The synergistic activity of these two sources of innervation is demonstrated in the mechanism of ejaculation

A possible additional motor innervation of the vesical neck by the pudendal nerve was suspected previously on the basis of beneficial results from pudendal intracaine blocks This procedure restored a balanced function to 56 traumatic cord bladders in 46 per cent of an earlier series and an additional 39 cases benefited in 41 per cent The dual innervation makes it understandable also why pudendal nerve blocks yield good results in combination with small transurethral resections of the vesical neck (11 cases 7 traumatic, 4 nontraumatic with restoration of function in 5 and 4 cases respectively), when a mild structural contraction of the vesical neck is combined with a functional contraction of the pelvic floor

The relaxation of the vesical neck on x-ray studies subsequent to pudendal

was then closed in layers with silk. Procaine penicillin, 300,000 units daily, was injected for 3 days and aureomycin was given twice a day by mouth at doses of 250 mg. There was no operative fatality.

Collection of the vesical secretion. At intervals which varied from 22 to 70 days after vesical isolation the abdomen was explored under ether anesthesia and the distended bladder was punctured with a needle and aspirated by means of a syringe using the most rigid asepsis. The fluid was cultured under aerobic and anaerobic conditions. Four dogs were sacrificed after collection of the fluid and the bladders were excised and fixed for histologic study by injection of Bouin's solution intravesically. In the remaining 5 cases a total cystectomy was performed.

The amount of vesical secretion and the chemical and cytologic data varied according to the presence or absence of infection (table 1). Of the 9 isolated

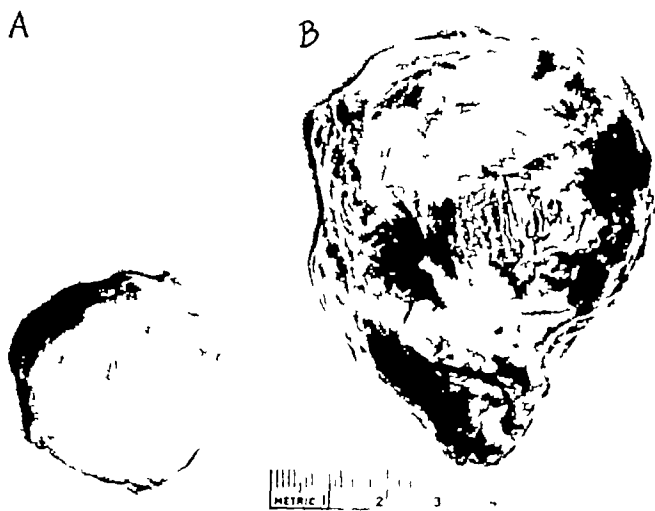


FIG. 2. Isolated bladder of dog 4, uninfected bladder with capacity 3 ml. isolated for 31 days. B, infected bladder containing 22 ml. pus, bladder has been isolated 43 days.

bladders (fig. 2) 2 were found to be infected and 9 were sterile on bacteriologic culture.

Cytology of the fluids. Erythrocytes and "ghost" erythrocytes in all. In each case the "ghost" erythrocytes predominate in number. Many small fat droplets in all. The fat droplets possess Brownian movement and stain with Sudan IV (neutral fat). Also there are many macrophages crammed with fat stainable with Sudan IV. No polymorphonuclear leukocytes. A few desquamated epithelial cells in each case.

The chocolate colored fluid consisted of about one-third cells. Upon centrifugation the supernatant "serum" was deep brown in color. Many macrophages containing heme-pigments were seen. Also clumps of amorphous heme pigments. In the chocolate colored fluids many oblong brown transparent crystals were observed, many arranged in parallel bundles. The size of the crystals was $10 \times 150 \mu$. Certain chemical analyses are reported in table 2.

The chocolate-brown pigment in the clarified supernatant was completely

caused by injury and one by an epidural abscess, the operative approach of Huggins, Walker and Noonan was used

The neurectomy was preceded by intracaine block of the pudendal nerves as a test of selection for probable response to neurectomy, in all cases pudendal anesthesia restored the bladder function temporarily

Highlights of anatomical data and the literature of pudendal neurectomy are reviewed

The bladder function became balanced after neurectomy

Electric stimulation of seven pudendal nerves was done on 4 patients and the vesical neck was observed during operation

Stimulation of the intact nerves or their proximal stumps was accompanied by vehement contractions of the pelvic floor, very weak contraction of the vesical neck and strong mass reflexes

Stimulation of the six distal stumps of the medial branch (perineal nerve) caused a distinct and strong contraction of the vesical neck in five instances, while only one of four stimulations of the distal lateral stump (dorsalis penis nerve) precipitated this response. The contraction of the perineal musculature was weak compared with that of the vesical neck and occurred but once with stimulation of the lateral distal stump suggesting the presence of Tavel's anomaly of innervation. Mass reflexes were absent with stimulation of distal stumps

The difference of response of the pelvic floor to stimulation of the intact nerves or proximal stumps and distal stumps respectively suggests that the pudendal nerve is of lesser importance for the innervation of the levator ani

The results of stimulation are discussed. They suggest a dual innervation of the vesical neck, by the presacral and pudendal nerves respectively. No clear line of demarcation can be drawn due to the intertwining of striated and smooth muscles of this region

The significance of a dual innervation for the physiology of micturition is discussed

The significance of the results is discussed for the patho-physiology of micturition and for the management of cord bladders

I wish to thank Dr. John D. French, Chief of Neurosurgery, Dr. D. C. Malcolm, Chief of Urology, and his staff, Drs. A. E. Comarr, Chester A. Conrad, D. H. Ewalt, John I. McGirr of my staff, and Mrs. R. L. Preddy for their valuable advice and actual assistance in preparing and illustrating this paper

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FIG 3 Section of bladder wall of normal dog



FIG 4 Section of wall of uninfected isolated (31 days) bladder, contents were 3 ml
See figure 2-4

which are usually better noticed in the apex of the papillae, are continuous and very easily appreciable

3. An additional change is also found in the muscularis in which the muscular fibers seem to lose their staining properties and appear pale and seem

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erythrocytes into methemoglobin which gave a chocolate color to the vesical secretion whenever it was present in significant amounts

Globules of fat are constantly present in normal vesical secretion and are observed either in isolated form or phagocytosed by macrophages

The presence of "ghost" erythrocytes and free heme-pigments in the fluid can probably be explained by the prolonged presence of erythrocytes in the bladder

The mechanism of vesical secretion can be explained by combined activities of diffusion, dialysis, transudation and diapedesis and attributed to the rich vascular and lymphatic supply of the normal vesical epithelium

CONCLUSION

The bladder of the dog secretes small amounts of fluid and the mucosa can oxidize hemoglobin

The author would like to express his deep appreciation for the technical advice and personal guidance which were given at all times by Professor Charles Huggins during the performance of this study

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The patient is placed in the lithotomy position. No attempt is made to excise the fistulous tract. A circular incision is made through the vaginal mucosa around the fistulous tract (fig 1). It is important to provide an adequate margin to use the vaginal mucosa as a "patch." The margins of the circumscribed vaginal mucosa are then freed. This dissection is carried out toward the fistulous tract and laterally. Mattress sutures of twenty-day No. 0 chromic are placed in a manner that results in an overlapping of the margins of vaginal mucosa inverting the mucosa so as to cover the fistula (figs 2 and 3). This forms a "patch" of inverted vaginal mucosa occluding the fistulous tract. The lateral margins of

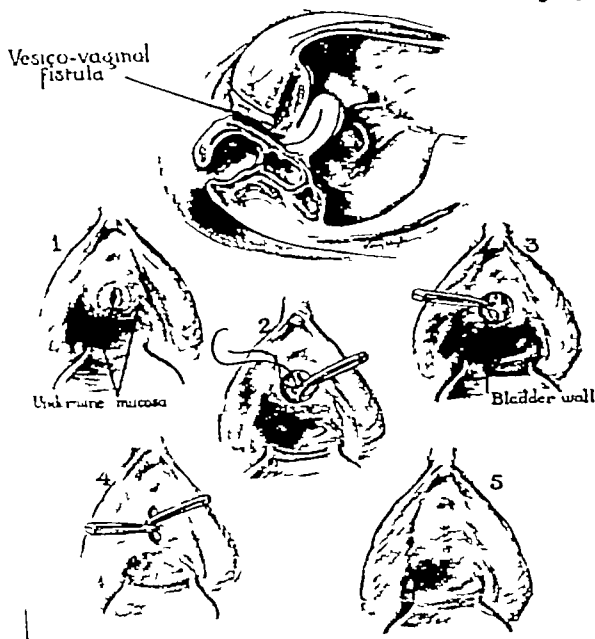


FIG 1

vesical mucosa which have been sufficiently undermined are brought together with interrupted chromic sutures (figs 4 and 5).

Postoperatively, the patient may lie in any position in bed. Continuous urethral catheter drainage is maintained using a 20F Foley catheter. The patient is usually ambulatory on the third or fourth day and the urethral catheter is ordinarily removed 10 to 12 days following surgery. Urinary antiseptics are routinely administered.

In observing these patients cystoscopically after operation, it can readily be seen that the defect in the bladder wall is occluded by the flap of vaginal mucosa which has a different appearance than that of bladder mucosa. The procedure obviates extensive dissection which often is impossible in patients who have had previous multiple operations. Too many sutures, superimposition of suture lines, or catgut in the vesical mucosa are avoided by the method described. Since

providing there is no muscle guarding or straining, and the abdominal wall is not too thick

Since it is common procedure in some urological clinics to treat acute urinary retention by the removal of 200 cc urine rapidly (to relieve pain) before slowly decompressing the bladder, we decided to observe a group of patients in acute urinary retention as to initial bladder pressure and the pressure change following the removal of 200 cc urine

It will be seen (fig 2) that the higher the initial bladder pressures, the greater the fall of pressure when 200 cc of urine are withdrawn. The bladder pressure following the removal of 200 cc of urine actually falls, at times, to less than one fifth of the original pressure. Obviously, as far as urinary hydrodynamics are concerned, the withdrawal of the initial 200 cc of urine should be as damaging as

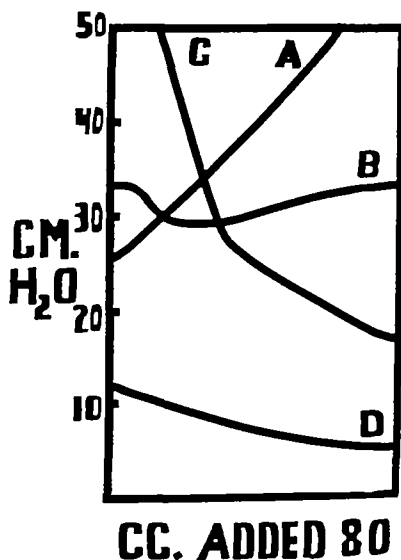


FIG 1

complete emptying of the bladder if the bladder pressure is above 30 cm of water pressure

Hryntschak and Creevy have stated that sudden decompression of acute urinary retention of all degrees is without immediate danger. Much of this reasoning has been based on the fact that hugely distended bladders containing up to 14 liters of urine have been rapidly decompressed without deleterious effects. No statements were made concerning the bladder pressures involved. It would seem logical that such greatly distended bladders would be most likely on the descending portion of the pressure-distention curve and hence the pressure concerned might be quite low. In fact, we have seen bladders with pressures of only about 5 cm of water although their contents measured four or five liters. Some of these bladders with such low pressures were seen in patients who had no previous history of urological disease but who had sustained head trauma. On the other hand, some of the bladders which contained less than 500 cc of urine had the highest pressures recorded (about 60 cm water pressure).

PHYSIOLOGY OF THE TRANSITIONAL EPITHELIUM OF THE URINARY TRACT I VESICAL SECRETION IN THE DOG

JOSE DE J. ALVAREZ-IERENA

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Considered at its simplest level the excretory passage of the urinary tract is a neuromuscular apparatus lined by transitional epithelium. The contractile elements of the tract have been considered rather extensively by other experimenters. Almost no work has been done on the function of the epithelial component. Does the lining of the urinary tract modify its contents? Is the bladder mucosa inert like a glass vessel which contains urine or does transitional epithelium secrete or absorb? These are the questions which we shall answer in the experiments reported in this thesis.

I ABSORPTION FROM THE URINARY BLADDER

The question of absorption by the vesical epithelium has been repeatedly studied by research workers. The first accurately performed experiment was carried out by Segalas, who in 1824 instilled a dilute alcoholic extract of *Strychnos nuxvomica* into the bladder and observed death of the experimental animal with convulsions 40 minutes after the beginning of the experiment.

Similar results were obtained by Maas and Pinner in 1881 and by Gerota in the latter part of the 19th century. Even up to more recent dates experimenters have been actively engaged in proving or disproving this resorptive activity.

The substances employed have been of miscellaneous nature and have included poisons (strychnin, potassium ferrocyanide, apomorphin), stimulating agents of the autonomous nervous system (epinephrin, pilocarpine), local anesthetic agents (cocain, procain, alypin), organic dyes (phenolsulfonephthalein, fluorescein, Indigo carmin) and anesthetic gases.

Results have been frequently contradictory but the most important data can be analyzed and summarized as follows:

1 *Reabsorption and endogenous products* In the frog, water is reabsorbed from the bladder if the cloacal aperture is closed by suture and the animal is exposed to a dry atmosphere (as in a desiccator) or to a hypertonic sodium chloride solution. When the frog dehydrated in this way is replaced in water, the bladder is again found to be full of urine. This absorption-excretion circuit was proved by Brooks Steen.

In mammals (rabbits, cats, dogs, etc.) urine is reabsorbed from the bladder if no emptying of its contents is permitted. Schär measured the volume of the vesical contents of dogs and the specific gravity, urea and chlorides were also determined. After this, the ureters were anastomosed to the skin and the distal stumps ligated. A catheter was inserted in the bladder and the urine was rein-

This investigation was aided by grants from Mr. Ben May, Mobile, Alabama, from the American Cancer Society recommended by the Committee on Growth, the National Research Council and from "La Nacional" Compania de Seguros sobre la Vida, Mexico City, Mexico.

The same results were obtained by Yutaka Saito with substances with higher molecular weight like cocain and alypin

The third factor involved in the resorption from the urinary bladder is the status of the vesical epithelium. It is on this point that the most intense controversies have been established. According to workers like Cohnheim "the normal vesical epithelium is impermeable to solutions." There are others like Streller and Vondra who believe that most of the positive results have been obtained due to trauma on the mucosa. This point has been invalidated by the excellent experiments of Mann and Magoun. They performed a bilateral ureterocutaneous anastomosis, ligated the vesical neck and one of the distal ureteral stumps and instilled the solutions through the opposite open ureteral distal segment. Thus they avoided any manipulation of the epithelium. Their work was performed using phenolsulfonphthalein (PSP) as indicator. Small amounts of this dye were absorbed from the bladder and excreted by the kidneys.

Streller and Vondra showed the numerical difference in the absorption ratio of a solution of urea expressed in percentage depending on whether this solution acted upon a normal or inflamed epithelium.

CONCENTRATION OF THE SOLUTION	NORMAL MUCOSA	TRICONITIS	MILD CYSTITIS
25%	0	1.1%	3.0%
10%	1.5%	10.6%	—
20%	4.0%	23.4%	25.28%

Mann and Magoun also showed that trauma or chemical irritation of the mucosa, as seen with the oral administration of cantharides, increases the absorption possibilities of the bladder.

Mann and Magoun concluded that "absorption takes place but only to a very limited extent" and this opinion coincides with the conclusions of Streller and Vondra who state that "the amounts resorbed from the normal bladder can be overlooked."

3 *Routes of absorption.* Since resorption from the bladder seems to have been demonstrated it remains to prove what route is followed by the absorbed substances. It is known since the original work of von Möllendorf that the bladder has 3 main capillary networks of blood vessels in the proximity of the vesical epithelium. One is found immediately underneath the basal row of epithelial cells, the second is in the structure called "the fibrillar layer" which German pathologists and anatomists describe between the mucosa and the submucosa. The third network is in the submucosa. The networks of lymph-vessels are only two: one for the mucosa and another for the submucosa.

It can easily be imagined that this anatomical situation is possible for re-absorption by either vascular or lymphatic route and von Möllendorf added the following remark to his anatomical description: "this remarkably close relationship between capillary networks and epithelium points towards the possibility that the urinary tract has other functions than the simple conduction of the manufactured urine."

and trauma, and when the bladder is rapidly decompressed we have observed kinking of the bladder vessels with its attendant thrombosis and secondary fibrosis. Slow decompression *may* minimize this kinking and reduce thrombosis and scarring. This problem will require further investigation.

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III TRANSFORMATION OF FIBROBLASTS INDUCED BY TRANSITIONAL EPITHELIUM

The experiments of Huggins on the influence of vesical epithelium in the transformation of connective tissue with resultant formation of bone have shown further aspects of the potentiality of this epithelium. He carried out implantation of portions of vesical mucosa in the fascia lata of the thigh or the sheath of the rectus muscle and noticed the appearance of an epithelial lined cysts at the seventh to ninth day. The adjacent connective tissue became edematous and deeply stained nuclei were seen in places on the sixteenth day, bone always developed surrounding a portion of the cyst and always adjacent to the newly formed mucosa. After ruling out the other vesical layers, the influence of gravity, etc., he proved with scrapings of vesical mucosa and with the transplantation of mucosa from the renal pelvis calyces and ureters that it was the epithelium which influenced the formation of bone whenever it was brought in contact with connective tissue. This experimental work has later been corroborated by other investigators.

IV VESICAL SECRETION

It has been previously mentioned that the anatomical distribution of blood and lymph networks is very rich in the basal area of the vesical epithelium. It has also been stated that only the trigonal glandular structures of the bladder possess gland-like structures. Nevertheless it seems that the excretory or secretory possibility of the bladder has neither been definitely established or ruled out and that the work done in this field has been carried out incompletely.

Kapusto and Dobrotvorsky have described cases of vesical malignant neoplasms which eliminated serous fluids in variable amounts. The presence of urine was excluded since these patients had bilateral ureteral anastomosis to the skin.

Nicolaux, Mauria and Novika reported in 1913 the passage of alcohol in both directions through the vesical mucosa, it could be excreted or absorbed. Schär performed some interesting dialysis experiments instilling concentrated solutions of urea into the bladder which was excluded from the upper urinary tract by bilateral ureteral cutaneous anastomosis. He noticed a marked increase in the liquid amount recovered from the bladder 24 hours after instillation.

Yutaka Saito reports similar findings. When sodium chloride solutions of less than 1 per cent concentration were instilled into the bladder there was excretion of sodium chloride through the vesical mucosa and when the solutions were of more than 1 per cent concentration the sodium chloride was absorbed from the bladder. In this experiment the bladder seems to react as a simple dialysis membrane. In another experiment Schär used distilled water, normal saline or 5 per cent dextrose solutions which were instilled into the excluded bladder. He recovered 30 minutes later a solution which contained 21 mg per cent of urea, and 4.5 mg per cent of calcium. Using larger intervals between instillation of the irrigating solution and its recovery and carrying out his experiments on uræmic dogs he reported the recovery of rather large amounts of urea, calcium, and chlorides.

The study of the mutual and reciprocal relations of the anatomical changes with the physiological phenomenon will help clarify some of the causes of urinary dysfunctions after prostatectomy. It is necessary to perform many postoperative urethrocytograms and to correlate roentgenographic findings with the patient's symptoms, urethrocytoscropy, cystometry, the rectal examination, the urethral calibration, and the urinary sediment to fully understand and utilize the diagnostic potentialities of this procedure. It is also advantageous to repeat urethrograms periodically and observe the changes that take place with healing. We can then establish if a roentgenographic finding is normal or pathological, temporary or permanent, and whether the appearance of the lesion changes with treatment and improved function.

Errors of interpretation of postoperative urethrograms have been and will continue to be made. Many are due to poor technique, faulty judgement or lack of experience. There are limitations to this procedure similar to pyelography. We have found our errors instructive and feel that with time and effort urethrography will rank in usefulness with other roentgenologic or urologic procedures.

This report covers an experience of over twenty years and is based on several hundred roentgenographic studies of patients who underwent every type of prostatectomy including multiple procedures. Lack of space prevents discussion of all sequelae and limits our presentation to frequent and important ones. The complications portrayed here are not all from personal cases, although we have had our share. Some of the patients were operated on at local and nationally famous urologic clinics, and the surgeons varied from enthusiastic resectionists to die-hard advocates of routine open prostatectomy.

The following points must be considered when interpreting the postoperative urethrocytogram:

- 1) The changes in the outline and shape of the bladder and the position of the base. With normal involution, the bladder contour becomes smooth as the trabeculations disappear, the shape changes from a convexity downward to a concavity downward and the bladder descends to the upper border of the symphysis and sometimes slightly lower.

- 2) The status of the prostatic cavity. The length, width, and deformities of the supracollicular urethra and its angulation and relationship to the bladder base vary following complicated and uncomplicated prostatectomy.

- 3) The presence or absence of the verumontanum. Its size, shape, and position, as well as evidence of vaso-deferential reflux, should be noted.

- 4) The configuration of the infracollicular portion of the prostatic urethra and the membranous urethra. There should be little or no change when the anatomy of this area is compared to the preoperative topography since surgery in this region is usually to be avoided.

- 5) The interior urethra. Any changes in the filling characteristics of the bulbous and penile urethra which were not present preoperatively must be considered a result of surgery or secondary to a complication.

The roentgenographic appearance of the prostatic cavity has many variations and the following chart is a classification of the factors which may normally alter the urethrographic topography after prostatectomy.

and A "stab" incision was then made high in the midline and the proximal end drawn through, the muscularis of the proximal stump was then sutured to the skin in several places. The principal incision was closed. By means of a thermocautery the end of the proximal stump was then transected.

Ureteral transplantation About 1 week after establishment of the colostomy the dog received sulfadiazine 0.5 gm twice daily and 300,000 Oxford units of procaine penicillin by daily injection for 3 days. The bladder was then isolated and the ureters were transplanted.

Under ether anesthesia the peritoneal cavity was opened through an incision 15 cm long in the lower right rectus abdominis muscle. The urinary bladder was delivered and with gentle upward traction the neck of the bladder and the

TABLE 1 *The infected bladders*

Number of Cases 2

Report of Culture *Escherichia coli* *Escherichia intermedium*

Gross description Purulent, homogeneous, dense fluid

Volume 22 ml, 63 ml

Acid phosphatase 12.2 King and Armstrong units/100 ml

Alkaline phosphatase 0.5 King and Armstrong units/100 ml

Phenolic substances (chromogenic substances with Folin Ciocalteu reagent) 19 mg

The fluid contained coagula of fibrin

Cytology The fluid contained motile bacteria and large numbers of polymorphonuclear leukocytes

The uninfected bladders

Number of Cases 7

Report of Culture No growth of aerobic or anaerobic bacteria

Gross description of fluids They fall in 2 categories, namely, light brown and chocolate fluid contents

Duration of experiment 22-70 days

Volume Light brown fluid 3-6 ml, chocolate fluid 10-16 ml

Duration of "chocolate fluid experiments" 41 and 46 days. Therefore the chocolate color does not depend on a long duration of the experimentation.

The fluids did not coagulate spontaneously.

prostate were brought into view. After incising the fat and peritoneum covering the gland, a traction suture was placed through the prostate and the neck of the bladder transected close to this gland. The distal end was closed with a continuous silk suture. The ureters were then isolated and transected near the bladder, the distal ends being ligated. The bladder was carefully emptied of its contents and the bladder neck sutured with a continuous suture of 000 catgut.

A catgut suture was then placed and tied in the proximal end of the right ureter. A tiny incision was made with a pointed knife into the lumen of the bowel and a grooved director inserted in the lumen, the needle bearing the ureteral suture was placed in the grooved guide to emerge from the bowel about 4 cm below the minute opening. The ureter was drawn into the bowel and the guide suture ligated. The small opening in the bowel was obturated by the ureter and no additional closure was necessary. The site of the urostomosis was covered with peritoneum. A similar procedure was done on the left ureter. The abdomen

urethral resection are funnel-shaped and do not extend down quite as close to the collicular region as with the open methods. Rapid and smooth involution of the prostatic cavity often occurs after the retropubic approach.

METHOD OF HEMOSTASIS

Prolonged excessive pressure by packs, bags or catheters on the prostatic bed interferes with the contraction of the cavity which appears large and dilated. Deep massive fulguration may cause edema and a marked irregularity of the cavity outline. The appearance on the urethrogram of the region of the vesical



FIG 1 A, intravesical prostatic hypertrophy, subsphincteric type. Base of bladder has been elevated without dilatation of vesical neck. B, prostatic cavity after enucleation. C, intravesical prostatic hypertrophy, transsphincteric type. Adenomatous prostate has projected through internal sphincter. D, prostatic cavity after enucleation. Note difference in appearance of vesical neck.

neck may be changed by the various suturing techniques used to control bleeding.

The degree of involution of the prostatic cavity varies in the same patient with the time which has elapsed since the operation. Shortly after surgery, the prostatic cavity appears relaxed, funnel-shaped, and irregular in outline. When the edema subsides and the superficial necrotic tissues are eliminated, the walls become less ragged and the cavity narrowed especially in its center. As the mucosa in the operated area regenerates, the supracollicular urethra further contracts and shortens and becomes smooth in appearance. Finally, the prostatic cavity involutes to a spindle shape with a slight dilatation in the middle third. Sometimes the prostatic urethra returns so completely to its normal size and

perceptible with trichloroacetic acid. It was instantly reduced to a red pigment with sodium hydrosulfite and more slowly by cysteine. This behavior suggested the presence of methemoglobin. Spectrophotometric examination in the Bechman Mode DU spectrophotometer revealed only slight deviation from the spectrum of undenatured methemoglobin. From the absorption at 500 m μ the concentration of methemoglobin in the fluid was determined as 1.92%. It is probable that minor amounts of hemoglobin or oxyhemoglobin are also present.

VI HISTOLOGIC MODIFICATIONS IN THE ISOLATED BLADDER

The transitional cell epithelium that lines the internal surface of the bladder is usually described as integrated by several layers of cells of different shapes (cylindric in the basal row and then polyhedric in the superficial stratus) (fig 3). The superficial layer has been described to exfoliate the polyhedric or slightly rounded cell which is usually seen in the normal urinary sediment. The number

TABLE 2 *Chemical analysis*

	LIGHT BROWN FLUID	CHOCOLATE FLUID*
pH	7.00	—
Water (gm per 100 ml)	94.58, 95.62	90.04
Solids (gm per 100 ml)	5.42, 4.38	9.96
Total N (mg per 100 ml)	658, 709, 869	1121, 1442
Non protein N (mg per 100 ml)	74, 108	140
Protein (gm per 100 ml)	3.65, 4.18, 4.38	6.78, 8.12
Chloride (mEq liter)	88.94	—
Glucose	—	72
Acid phosphatase, units, 100 ml	4.9, 8.4, 9.0	1.1, 3.6
Alkaline phosphatase, units, 100 ml	0, 0, 1.2	0.5, 1.4
Phenol, mg 100 ml	10, 15, 18	24, 57

* Supernatant serum after centrifugation

of rows of layers of epithelial cells which integrate the epithelium have been described to diminish with vesical distention and to augment with the formation of the rugae after evacuation of the bladder.

What modifications are caused on their cellular pattern by the functional exclusion of the bladder from the urinary tract? According to our findings the result varies according to the presence or absence of infection.

If infection is not present the general appearance of the vesical epithelium is only slightly modified by the following changes:

1. There is an increase in the amount of layers of epithelial cells as compared with the non-isolated bladder and the large polyhedric or circular cells (which constitute the most superficial row and which normally have an imprecise delimitation) are much smaller in number and frequently absent (fig 4).
2. There are also certain changes in the submucosa which seems to lose its normal smooth papillary pattern to turn into an almost continuous line. The fibrillar cells described between the epithelium and the submucosa,

shape that it is difficult to realize from the urethrogram that a prostatectomy has been performed

URETHROCYSTOGRAPHIC FINDINGS IN PERSISTENT PROSTATISM AFTER PROSTATECTOMY

Urethra	{	Infection Stricture Calculus Diverticulum Foreign body Trauma	{	Urethritis Peri-urethral abscess Cowperitis Fistula Extravasation False passage	
Prostatic cavity	{	Non-involution	{	Residual prostatitis Calcification Scarification Carcinoma	Prostatic bed
	{	Residual tissue	{	Prostatectomy Hypertrophied commissure Adenomata	{ Retained lobes Apical masses Tubular stumps Anterior Posterior Subtrigonal Suburethral Subcollicular Extension
	{	Extracapsular trauma	{	Subtrigonal Infracollicular Perineal Suprapubic Retropubic	Extravasation
External sphincter	{	Neurogenic Scarification Traumatic	{	Absent Atonic Hypertonic Intrinsic Extrinsic Intra-urethral laceration Extra-urethral injury	
Vesical neck	{	Obstructed	{	Hypertrophy of bladder wall Hypertrophy of trigone Surgical incision Neurogenic Non involution	
	{	Fixed	{	Sutured Sclerotic Spastic	

to diminish in number. This is interpreted as an atrophic reaction due to lack of normal contraction.

In the presence of infection there are very marked changes in the histology (fig 5) of the vesical epithelium. Two dogs developed intravesical infection after the isolation of the organ and in their bladder the following changes are observed:

- 1 The transitional epithelium appears as a stratified pattern of large, polyhedral, vacuolar cells with large pale nuclei which are at times even impossible to visualize but with deeply stained nucleoli.
- 2 The submucosa turns into a dense fibrillar pattern which is particularly

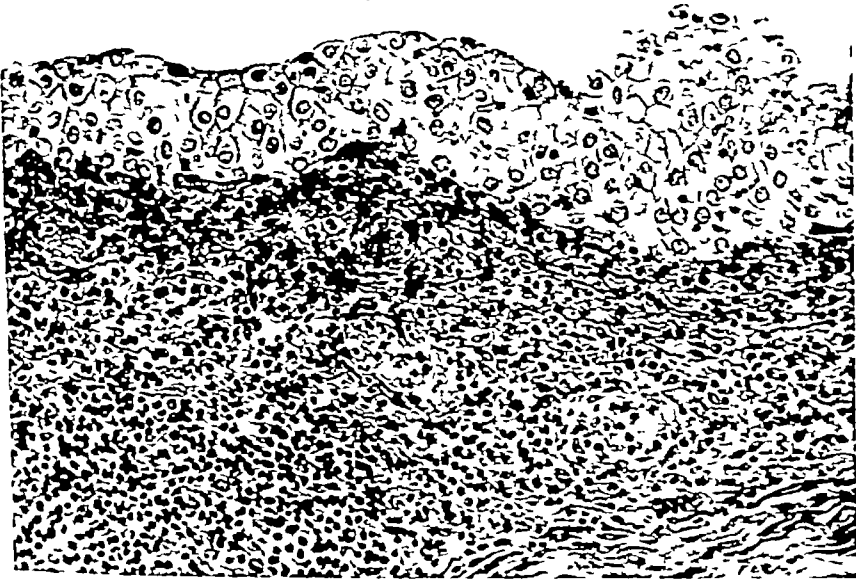


Fig 5 Section of infected isolated (43 days) bladder, contents were 22 ml. See figure 2, B

dense around the blood vessels and which shows infiltration by very large numbers of polymorphonuclears and lymphocytes.

- 3 The infiltration is particularly intense in the muscularis.

SUMMARY

The normal vesical epithelium has a secretory activity.

The amounts secreted in a noninfected bladder varied between 3 to 16 ml and did not seem to have a parallelism with the time of the experiment.

The normal vesical secretion is liquid and does not coagulate spontaneously.

The vesical secretion contains proteins, chlorides, total and nonprotein nitrogen, acid and alkaline phosphatase and in one instance glucose. These are chemical components of normal plasma found in similar amounts in the secretion, except for a slight elevation of its acid phosphatase levels and for the considerable amount of nonprotein nitrogen.

The normal vesical epithelium oxidized the hemoglobin present in normal

encountered in this type of approach and seldom seen in open surgical intervention. Failure to recognize small perforations may lead to perivesical, periprostatic, or peri-urethral infection with eventual massive scarification and interference with bladder function. A urethrogram at the time of operation will show the site of the perforation and the extent of the extravasation, and a follow up will demonstrate the closure of the defects. We have also used urethrocytography to check the eventual end results of these perforations on an anatomic and physiological basis. We can visualize the integrity of the luminal continuity and note the rigidity or mobility of the vesical neck and the external sphincter.

PROSTATIC CAVITY

The normal involution of the prostatic cavity has been previously described.⁴ Failure to involute or delay in involution is frequently noted on the urethrogram.



FIG. 4. A, note urethral diverticulum observed after prostatic surgery. B, urethrogram 1 month after surgical removal of diverticulum. Note urethral fistula which eventually closed.

taken a few weeks or months after surgery. With persistent infection, the prostatic cavity appears atonic and the outline is irregular. The region of the vesical neck is dilated and the bladder and urethral outline appear contiguous with little or no markings to differentiate the region of the internal sphincter. Non-involution has been observed with excessive scarification in the prostatic cavity. The supracollicular urethra appears as an irregular fusiform deformity which on the voiding urethrogram is fixed and with limited distensibility. Calcification gives a similar picture except that the calcified deposits in the retained capsule can be visualized.

Carcinoma of the prostatic bed will prevent involution and often produces a bizarre urethrogram.

Residual tissue is an important cause of prolonged morbidity after prostatectomy. Shivers and Groom⁵ found that residual prostatic tissue occurred in 53 cases or 3.6 per cent, and noted that there was a higher incidence following resection (1.4 per cent) than after open surgery.

⁵ Brodny, M. L. and Robins, S. A. Morbidity after prostatectomy. A urethrocytographic study. *J. Internat. Coll. Surg.*, 14: 143-158, 1950.

OBSERVATIONS ON DYNAMICS OF ACUTE URINARY RETENTION IN MAN

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In a previous report (Lawson and Tomlinson) it was shown that when dogs are subjected to acute urinary retention the pressure in the dog's bladder increases to a peak as the bladder is distended, then decreases although bladder volume is constantly increasing.

It was also found that if saline were added to the distending bladder, the pressure changes subsequent to the addition of saline would depend upon the portion of the curve represented at that time. For example, if the pressure observed were on the ascending portion of the curve, the addition of saline would cause the bladder pressure to increase sharply. If the plateau of pressure had been reached, the pressure observed following the addition of saline would remain essentially constant, likewise, if the pressure observed represented the descending portion of the curve the additional fluid would cause a sharp fall in bladder pressure.

For obvious reasons the dog experiments could not be completely reduplicated on humans and hence the continuous production of a pressure-distention curve such as seen in the dog experiments could not be obtained. However, since all degrees of bladder distention are seen in medical patients, pressures could be observed which should correspond to all portions of the pressure-distention curves seen in the dogs, providing such curves obtain in human bladder distention.

Since the dog experiments demonstrated that the portion of the curve involved at any given pressure could be determined by the addition of saline to the distending bladder, it was decided to apply this approach to human bladders in various stages of distention. The results of these studies are shown in figure 1.

Graph A shows the effect of the addition of 80 cc of saline to a bladder on the ascending portion of the curve. Graph B shows the effect of adding 80 cc of saline to a bladder on the pressure plateau. Graphs C and D show the effect of adding saline to bladders representing the descending portion of the curve.

From curves of the above types, one may demonstrate that the human bladder has distention characteristics similar to those seen in dogs.

Although 80 cc of saline were added to the experiments recorded, 10-15 cc of saline were found to demonstrate similar pressure changes. Therefore, the portion of the pressure-distention curve involved at any moment during urinary retention can be demonstrated by the addition of small amounts of saline to the bladder.

In actual clinical practice one can determine bladder pressure by attaching a small length of sterile transparent flexible tubing to the inserted catheter by means of a glass adapter and observing the height to which urine rises in the tubing above the level of the bladder. Furthermore, with practice, bladder pressure can be fairly well estimated by palpation of the distending bladder,

EXTERNAL SPHINCTER

The adequate external sphincter is the main mechanism in the control of continence. On the urethrogram, the external sphincteric markings cannot be sharply delineated distally from the membranous urethra or proximally from the prostatic cavity, but the changes in its width, shape and outline, and the degree of rigidity or mobility often contribute valuable diagnostic information. The hypertonic external sphincter may make retrograde urethrography very difficult, the spasm preventing the passage of the opaque medium into the prostatic cavity. If pressure is continued, urethrovenous reflux may occur. Sometimes the spasticity is functional and can be overcome by deep breathing or diverting the patient's attention. A spastic external sphincter may be secondary to pathological changes in the bladder or in the anterior urethra. Muscular atony



FIG. 6. Vesical neck hypertrophy and suprapubic fistula. Bladder failed to heal due to obstruction at bladder neck.

city and relaxation of the external sphincter are often seen on the urethrogram of the first voiding after a patient has been on postoperative constant drainage for a period of time. The prostatic cavity appears irregular, the sphincters are poorly demarcated, and the entire urethra is dilated. A repeat urethrogram 2 to 4 weeks after the return of continence will show a smoother and smaller prostatic cavity, a well outlined external sphincter and increased tone of the entire urethral canal.

Persistent atonicity and even absence of contraction of this area has been observed frequently with postoperative incontinence. On the urethrogram the area appears as an almost straight undifferentiated tube.

The external sphincter is frequently traumatized and the injury can be visualized on the urethrogram. Damage to the external sphincter may occur in five ways: 1) intra-urethral, a portion of the membranous urethra is accidentally removed during suprapubic prostatectomy, 2) extra-urethral, the external sphincter is exposed in the perineum and injured during a perineal prostatectomy, 3) neurogenic, the sphincteric nerves that traverse the capsule of the gland on its lateral aspects are injured, resulting in anesthesia and paralysis of the

It has been inferred in the past by some investigators that any bladder can be rapidly decompressed without immediate danger. This is based on the fact that hugely distended bladders have been rapidly decompressed without harmful sequelae. This is a "non sequitur" conclusion, because small bladders may have very high pressures, whereas huge bladders may have very low pressures.

Comprehension of these basic physical principles may help explain why we find two opposed groups of urologists: one group proposing rapid decompression of all acute retention, and the other stating the observed occurrence of post-retention anuria and "bladder shock" following rapid decompression.

During our study we observed no harmful results from sudden decompression of all degrees of bladder distention. However, reactions to sudden decompression definitely can occur and in retrospect in our clinics those reported were in patients with smaller bladder volumes. Also, there has been no evidence of so called post

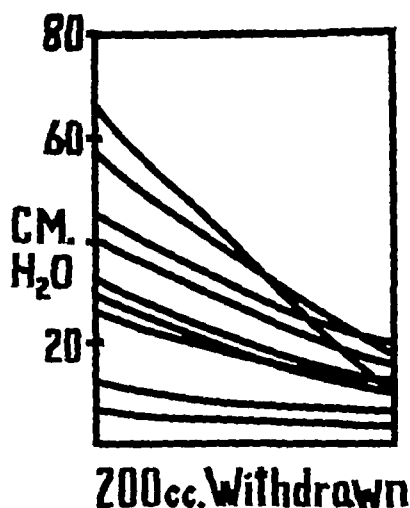


FIG 2

evacuation splanchnic pooling with its subsequent changes in pulse and blood pressures either in dogs or man.

It is our opinion, on the basis of experimental data, that the attitude of treating a greatly distended bladder more cautiously than a smaller one with regard to bladder shock and post-retention anuria is incorrect if not dangerous. However, on occasion, hugely distended bladders will show submucosal and mucosal thromboses and hemorrhages. Subsequent care with regard to prevention of infection in such traumatized bladders is therefore mandatory.

Another observation which may be of significance with regard to rapid versus slow bladder decompression was the fact that when canine bladders which had been subjected to great degrees of distention were decompressed rapidly many thrombosed vessels were found in the bladder wall. Subsequent to thrombosis there was fibrosis of the bladder. Indeed, repeated bladder distentions were utilized to produce fibrotic bladders for the determination of kidney secretory pressures.

DISCUSSION

DR SAMUEL A VEST (Charlottesville, Va) Drs Brodny and Robins are to be complimented for stressing this important feature of prostatic surgery. Sequelae and the persistence of the symptoms of prostatitis are far too common an occurrence. The authors are also to be commended for their thorough and persistent search for the causes producing such symptoms following this type of surgery. They have also been in the forefront in the use of cysto-urethrograms for the recognition of the many anatomical changes that occur postoperatively. All of us recognize that in urological surgery our job is only half done at the operating table. We can and must be of great service to the patient during the relatively long convalescent phase.

A few years ago in our clinic we did about 150 cysto-urethrograms following prostatic surgery. We used either rayopake or 15 per cent sodium iodide as a contrast medium but with some difference in technique from that of the authors who inject their material through the urethra with the use of an ingenious clamp. In our experience we soon found that it is better to instill the opaque material in the bladder through a catheter and then obtain upright x-rays with the patient holding the dye as well as during the act of micturition. We concluded that such "action" x-rays are more informative and have implications in physiology. This was particularly true in the study of the bladder and vesical neck dysfunction.

Our conclusions in general corroborate those of Drs Brodny and Robins with some admitted differences. We do not concur with the authors as to the value of cysto-urethrograms as a routine procedure following prostatic surgery. The prostatic fossa in some instances may be visualized to advantage but in general cysto-urethrography is not as reliable in recognizing small remaining lobes of tissue as is cystoscopy. Indeed, false filling defects have been seen in cysto-urethrograms which may mislead the observer. These are apparently due to fixation of the capsule which is infected and fibrotic following electrocutting procedures.

The prostatic fossa following open surgery is somewhat different in appearance than that following transurethral resection. In the former the capsule tends to collapse forming a more or less small fusiform tube of the prostatic urethra while following transurethral resection the capsule tends to be rigid resulting in a large, more cavernous interior. A patient who voids in adequate stream with good control and who empties his bladder without symptoms may be considered a good operative result without further detail study. Indeed, the anatomical sequelae are not always proportionate to the symptoms. We have encountered marked symptoms without abnormal anatomic findings and vice versa. For other patients who do not make satisfactory progress a simple and relatively painless panendoscopy (McCarthy No 20 panendoscope) will often reveal remaining glandular tissue or other causes for the symptoms. Cysto-urethrography in our opinion is not a complete substitute for routine cystoscopy when some form of

between observed bladder volume and bladder pressure (fig 3) The elastic characteristics of the bladders studied were highly variable so that no overall correlation could be made between the portion of the pressure-distention curve involved and the bladder volume at any particular moment This is most probably explained by the fact that the urological lesions were diverse Hence, in a bladder with dilatation secondary to prostatic hypertrophy the peak pressure was observed to occur much later with regard to bladder volume than in retention secondary to head trauma where no previous urinary tract disease existed However, if only bladders which were normal before retention occurred are considered, the co-efficient of correlation is about .67, showing fairly good volume-pressure correlation in normal bladders during distention

SUMMARY AND CONCLUSION

The distention characteristics of human urinary bladders are found to be similar to those of canine urinary bladders

The portion of the pressure-distention curve involved in any given cases of acute urinary retention can be determined by adding 10-15 cc of saline and observing the resultant pressure changes

The higher the observed bladder pressure before 200 cc of urine was removed, the greater will be the fall of pressure subsequent to its removal Depending on the height of initial bladder pressure, the withdrawal of 200 cc of urine can cause the bladder pressure to drop to less than one-fifth of its original value

The statement that greatly distended bladders should be decompressed more carefully than small bladders does not hold true either theoretically or in actual practice, with the exception that in some greatly distended bladders submucosal thromboses and hemorrhage may make certain precautions necessary as regards the prevention of subsequent bladder infection

The recording of bladder pressure at the bedside can be carried out easily by attaching transparent sterile tubing to the inserted bladder catheter by means of a glass adapter, and observing the rise of urine in the tubing which is held above the level of the patient's bladder

When in doubt about decompression of urinary retention in a patient, the pressure should be recorded and if above 30 cm of water pressure the bladder should be decompressed slowly "ab initio"

There is no patient-to-patient correlation between bladder volume and bladder pressure and no overall correlation between observed bladder volume and the portion of the pressure-distention curve involved at this volume However, if one only records the pressure-volume relationships in normal bladders during distention a co-efficient of correlation of approximately .67 will be found, showing fair pressure-volume correlation for normal bladders undergoing distention

Many cases of post-retention anuria or oliguria may well be explained on the basis of swelling of the kidney parenchyma with its subsequent increase in intrarenal pressure Hence the method of decompression may not be primarily responsible for the anuria, but rather the disruptive changes within the kidney due to urinary back pressure

In great degrees of bladder distention there is considerable vascular stretch

the prostatic capsule closure in the usual manner, bringing the suture to the midportion of the incision and then placing another suture in the opposite corner, carrying the two sutures to the midportion of the incision, where they are tied. This gives a tight closure, and is a simple procedure.

DR. BRODNY: I should like to make some comments on Dr. Vest's observations.

First, we use both the voiding and retrograde methods of urethrography, and believe that their indications are in many ways comparable to those for retrograde and excretory urography. Each has specific advantages, and if you will do both procedures on the same patient, you very rapidly become aware of their supplementary and complementary values.

The cost of urethriograms is an important economic factor, but I think that the monetary losses which occur secondary to the disabilities produced by persistent symptoms are far greater.

If you will routinely do what Dr. Vest has done—study a series of prostatectomies urethrographically after surgery—considerable interesting diagnostic information may be obtained.

It is true that a patient is sometimes seen with pathological changes of the prostatic cavity, and the patient is relatively asymptomatic. It seems a little confusing until you think, for example, how often hydronephrosis may give no symptoms, and how often you see a silent stone in the kidney.

Some of the pathological lesions in the prostatic cavity are important only as they interfere with urination. I have seen a large retained lobe in the prostatic urethra give no symptoms. You often see this after an inadequate transurethral resection. On the other hand, a little piece of prostatic tissue left in the vicinity of the external sphincter or at the vesical neck may cause a good deal of urinary dysfunction.

One other point. I noticed from Dr. Vest's slides that most of his urethrograms were in the anteroposterior view. It is important to study the patient from the oblique view. A prostatic lesion is often missed on the anteroposterior view, but is easily visualized if the oblique view is taken.

Just one word about Dr. Bell's reference to sutures in the prostatic cavity. Those urologists who do open resections of the vesical neck and do suturing inside the prostatic cavity will find that urethrography, both voiding and retrograde methods, is valuable to observe the physiological effects of that particular type of resection and suturing.

RHABDOMYOSARCOMA OF THE BLADDER

VERNON H YOUNGBLOOD, RAFE BANKS, JR AND E E DENNEY

From the Department of Urology, Grady Memorial Hospital and Emory University School of Medicine, Atlanta, Ga

Rhabdomyosarcoma of the urinary bladder is an extremely rare tumor and usually a fatal one. In a search of the literature, 12 such cases were reported. Statistics in such a short series are unreliable but do show a trend. Including the case that we are presenting, 11 of 13 cases were in children of ages from 1 day to 33 months. The average age was 17 months when first seen. The sex differential was not significant. The other 2 cases occurred at ages 32 and 69. The main symptoms were straining on urination and defecation, incontinence, hematuria, frequency and urinary retention, and palpation of a mass in the bladder in four instances. One case has been reported as living, 6 months postoperatively. The remainder have rapidly succumbed to local recurrence and extension of the tumor in an average of 6 months. The adult of 69 is the only case reported having distant metastases.

There are several possible explanations for the occurrence of a striated muscle sarcoma in the smooth muscle wall of the bladder, but most writers agree that a developmental defect at the end of the wolffian duct allowed cells destined for the striated muscle of the anterior abdominal wall to be misplaced in the bladder wall.

CASE REPORT

J R, G M H No 336851, a 33-months-old Negro female child, was admitted to Grady Memorial Hospital on February 24, 1950, with a 4-weeks' history of nocturia, dysuria, incontinence of urine, and straining and pain on urination and defecation. At the time of onset of these symptoms, the family doctor found the urine to contain innumerable red blood cells and 4+ albumin. Two weeks after onset the patient was seen in the outpatient department of Grady Memorial Hospital, an excretory urogram was interpreted as normal. A bladder filling defect was erroneously thought at that time to be due to rectal contents (fig 1). With no improvement, the child was admitted for further study.

Examination revealed an alert, intelligent, and healthy appearing child. The history was negative except as stated, development was normal, sphincter control was normal since the age of 15 months. Physical examination was negative except for a fairly well defined suprapubic mass arising about 2 finger breadths above the pubic bone. Blood count and nonprotein nitrogen determinations were normal. Urinalysis pH 7.5, specific gravity 1.014, albumin 2+, microscopic 50-60 red blood cells, 5-8 white blood cells and 4-6 atypical epithelial cells. One of us (E E D) thought that the atypical epithelial cells appeared to resemble tumor cells, and on this basis along with the presence of a suprapubic mass a tentative diagnosis of tumor of the bladder was made.

Cystoscopy on February 25 showed a tumor mass filling most of the bladder. It appeared to be attached to the roof of the bladder and had the appearance of

rather than pain. If he is cognizant of urological ways, he hopes to be free from the necessities of sounds and bougies, of irrigations and instillations, and most pressing of all, he hopes to be free from threats of "second sittings" and repeat operations. He hopes to be through with urologists, for once and for all. Our query here is, "How often, 5 years after prostatectomy, can the patient be said to have realized these hopes?"

Certainly, there is an abundance of statistical material from which one might expect to gain the answer. There is no shortage of careful follow-up evaluations which have emanated from the perinealists, the transurethralists, and the devotees of the suprapubic school. Today we, in this country, are just entering that period in which any appreciable number of retropubic prostatectomies have been followed for 5 years but we may confidently expect equally painstaking evaluations on this score. But, after devoting careful attention to such reported series, we have felt an inescapable conviction that the answer which we seek has eluded us. We seem to come much closer to the type of information we desire if we read over individual case histories from patients who have undergone prostatic surgery.

It seems to us that there are several interesting and pertinent reasons why it remains difficult to assess the late results of prostatectomy. First and foremost is that partisanship has intruded upon science in this most controversial of surgical fields. It does not follow that this partisanship has been bad. It has unquestionably played a major role in stimulating the rapid advances in the development of the divergent techniques. But partisanship which tends to gloss over disadvantages, minimize shortcomings, and magnify virtues (real or assumed), distorts the literature concerning prostatectomy to a significant degree. In spite of all the data which have accumulated over the years as to the merits of the various approaches, it remains a fact that where a youngster takes his training is likely to determine the type of prostatectomy he will prefer. There is still a strong tendency for the perineal advocate to assume the rather superior attitude that the intricacies of the anatomy of the perineum are beyond the range of the average surgeon. The resectionist is prone to scoff at the devotees of open surgery as lacking in the instrumental dexterity that is the *sine qua non* of good resection. The retropubic enthusiast looks on the others as conservative old guffers afraid to tackle a new and superior method. All three look down upon suprapubic enucleation with the implied attitude that anyone can "junk" out a prostate by the roots and pray that pressure will stanch his hemorrhage. But, of course, the chap who has practiced suprapubic enucleation to his eminent satisfaction for these many years smiles tolerantly at the great technicians who have to find a hard way to do an easy job.

In recent years, there has been a reaction to this type of partisanship, and it has become more popular to advance the view that the well rounded urologist should be a master of all approaches to the prostate, that the operation should be fitted to the case, and that, under such circumstances, the patient will be best served. It has seemed to us that there can be no valid quarrel with this middle ground. If, in a given case, one technique offers advantages not possessed by the others, then obviously that is the technique of choice. But here again we come

URETHROGRAPHIC TOPOGRAPHY AFTER PROSTATECTOMY VARIES WITH

A Type of Prostate	Size	1 2 3 4
	Shape	- Intra-urethral - Intravesical - Intrarectal - Combined - Vesical Neck
	Pathology	- Adenomatous - Fibrotic - Carcinoma - Calcified
B Method of Prostatectomy	- Suprapubic - Perineal - Transurethral - Retropubic - Vesical Neck Resection	
C Method of Hemostasis	- Hemostatic Catheter - Prostatic Bag - Fulguration - Pack - Suture	
D Time and Degree of Subinvolution		

TYPE OF PROSTATE

The type and size of the prostatic gland will affect the size and shape of the prostatic cavity. We have previously described the roentgenographic anatomy of the normal male urethra and reported a classification of the types of prostatic obstruction based on the distortion of the urethrographic topography.¹ The anatomical differences which the character of the obstruction will make on the postoperative urethrogram are illustrated in figure 1. The type of vesical neck and its surgical treatment will especially alter the shape of the area of the prostatic cavity contiguous to the bladder. The pathology of the prostate may also change the postoperative pattern of the posterior urethra. After the removal of a fibrotic or a calcified gland, the cavity will remain more rigid and involute slower than with the adenomatous prostate.

METHOD OF PROSTATECTOMY

The surgical approach to the prostate affects the prostatic topography (fig 2). After the transurethral method (fig 3), the prostatic cavity often is not as smooth as following the open operation and may not involute as rapidly or completely, especially after deep fulguration. Many of the postoperative cavities after trans-

¹ Brodnv, M. L. and Robins, S. A. Prostatic obstruction. A urethrocytographic classification. *Revista de Urol*, 8: 162-172, 1950.

endoscopic resections. Otherwise, they are likely to live to require further prostatectomy. Only the fact that our series includes such cases where the initial resection was done by admitted masters of the technique reassures us that it is not wholly a matter of our own inadequate resections.

The second consideration is persistent infection. Here again, we find that our greatest trouble lies with those cases that were initially resected. Discounting those that have obstructive tissue still present, and concentrating only on those that have been adequately relieved of obstruction, as judged by the absence of residual urine, it seems unlikely that there is any major difference between resection and open operation on this score. In those cases, the major cause seems to be the co-existence of diverticula. Since diverticula can only be handled adequately by direct exposure and mobilization of the bladder, our hindsight dictates that we could only have cured these patients by doing a combination diverticulectomy and transvesical enucleation or doing a two-stage procedure. It is our feeling that in most instances where diverticula are large and not too numerous, they may be excised along with the prostatectomy. We should be inclined then, to say that when the prostatic obstruction and the diverticula may reasonably be tackled in one session, the job should be done suprapubically. When there are good reasons for making a two-stage procedure of it, we should be inclined to favor perineal enucleation of the prostate or transurethral resection as the first stage in order to facilitate the operative approach and mobilization of the bladder at the second stage.

The third consideration is stricture of the urethra. This is predominantly a complication of resection, but it is to be freely admitted that judicious use of perineal urethrotomy may minimize this, as may the use of adequate meatotomy. We have seen a number of instances in which the patient had as much disability from the postoperative stricture as he did originally from the vesical neck obstruction. Our hindsight would lead us to conclude that if we had it to do over again, we would either do open surgery, or would so modify our transurethral technique as to attempt further to avoid the stricture formation. Our impression is that if the urethra does not readily accommodate instruments of the size of the resectoscope, we had better discard the thought of resection and lean toward open operation.

A fourth consideration might be the preservation of sexual potency. There are numerous examples of well-preserved potency following any of the techniques of prostatectomy, but it is our impression that more patients question us as to whether or not their departed sexual powers will ever return when the operation was done by the suprapubic or perineal route. In consequence, when this factor looms up as of importance to the individual, we are inclined to consider the applicability of endoscopic resection or retropubic enucleation.

We should like to conclude with one further thought on the subject of indications and contraindications for the various types of prostatectomy. The fact that the young surgeon learning the technique of resection will probably rupture the bladders, or will do a few over-enthusiastic extirpations of tissue including some of the external sphincter, is not an indictment of the method. It is equally true

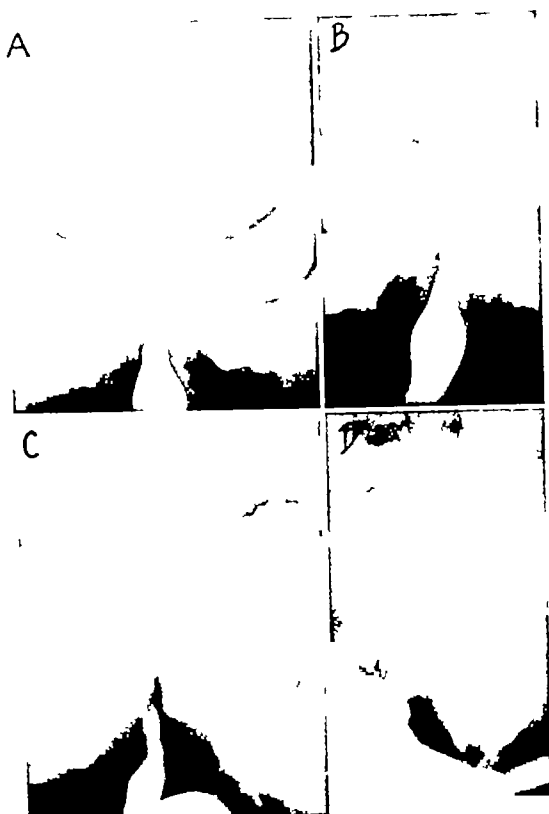


FIG 2 A, preoperative urethrogrm showing large intravesical prostate of subsphincteric type B, urethrogram 1 year after suprapubic prostatectomy. Good functional result C, preoperative urethrogram shows a small atrophic prostate. Note diverticula D, urethrogram 2 years after perineal prostatectomy. Diverticula involuted without surgery. Good functional result

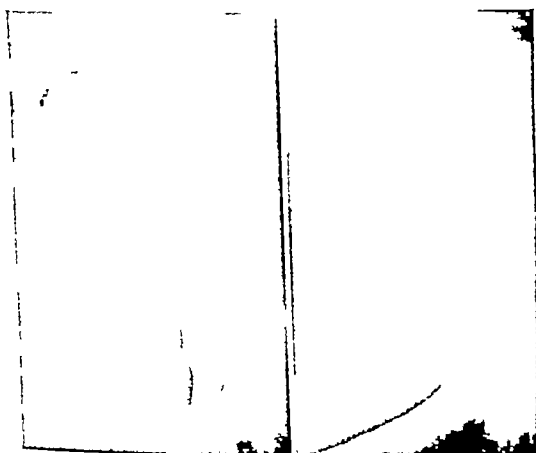


FIG 3 Postoperative urethral stricture and abscess of bulbo-urethral gland. Trans-urethral prostatectomy. September 4, 1950. Urethrogrm performed 1 month after surgery. Difficulty in voiding. Painful mass developed in perineum and required incision and drainage. Note that abscessed gland and its duct are filled with opaque medium

LABORATORY CONTROLS IN CARCINOMA OF THE PROSTATE ESTROGENIC AND ANDROGENIC EFFECTS

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Various enzyme systems of the serum are known to be influenced by metabolic disturbances accompanying active malignant growth. One of the better known examples of this is acid phosphatase. This enzyme is increased markedly in prostatic adenocarcinoma after extension beyond the capsule has occurred^{1, 2}. Estrogenic therapy or orchiectomy is usually followed by considerable decrease in acid phosphatase enzyme. The procedure is rather complicated and reliability of results seems to be a gift accruing to only a few technicians.

Alkaline phosphatase determinations have been used similarly as a measure of bone sarcoma activity although it is at once apparent that such studies can be applied only in cases in which the diagnosis of malignancy is proved.

Recent work with proteolytic enzymes and their inhibitors has yielded information of value in determining the activity of a wide variety of neoplasms. Like the foregoing mentioned enzymes, these also are nonspecific and not diagnostic for cancer. They are, however, quite sensitive in detecting the responsiveness of a neoplasm to therapy. In applying this method of charting tumor growth rate it is, of course, imperative that the case be uncomplicated by factors which in themselves could influence the results. Single determinations are of little value as is the case with acid phosphatase. Prognostication as to the activity of neoplastic diseases obtains only with the trend gained from many determinations.

Representative inhibitors of two groups of proteolytic enzymes have been studied most intensively. Chymotrypsin was selected from the trypsin group while rennin is a representative of the pepsins. Each has been scrutinized most intensively and considerable purification of the active factors has been obtained. The enzyme inhibitors are probably proteins.

A delicate and constant balance is normally maintained between rennin and chymotrypsin inhibitors. Rennin inhibitor of 8-10 units and chymotrypsin inhibitor of 3-5 units are the usual values for healthy adults. Rennin inactivator is much greater in the growth and developmental phases of individuals, while the chymotrypsin inactivator concentration remains constant for all ages.

Traumatic incidents, surgical intervention, pregnancy, acute and chronic

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Read at annual meeting, American Urological Association, Chicago, Ill., May 21, 1951.

¹ Woodard H. Q. and Dean, A. I. The significance of phosphatase findings in carcinoma of the prostate. *J. Urol.*, 57: 158-171, 1947.

² Huggins C., Yu, S. T. and Jones R., Jr. Inhibitory effects of ethyl carbamate on prostatic cancer. *Science*, 106: 147-148, 1947.

³ Nesbit, R. M. and Blum W. C. Serum phosphatase determinations of prostatic cancer. Review of 1150 cases. *J. A. M. A.*, 145: 1321-1323, 1951.

Bladder	{	Diverticulum	
		Hypertrophy of interureteric ridge	
		Calculus	
		Fistula	
		Tumor	
		Neurogenic	
Idiopathic	No structural lesions	{	Hysteria
			Neuresthenia
			Etc

URETHRA

Infection Persistent postoperative urethritis is a complication of prostatectomy whose importance may be overlooked. The infection often causes symptoms by invading the folds and glands of the mucosa and urethral adenexa. Figure 3 is a case of cowperitis following transurethral resection. Chemotherapy often temporizes but does not eradicate these foci. Inflammatory edema and secondary overgrowth of fibrous tissue with eventual contraction may cause a narrowing of a large portion of the urethral canal. We have previously described the urethrographic findings of infection of the male urethra.^{5, 6}

Urethral strictures Strictures are the most common complication causing urinary difficulty after prostatectomy. Although they respond to repeated dilatation, they require attention for a prolonged period of time and in many cases produce undesirable economic and emotional problems. Many of these strictures are avoidable and every effort should be made to prevent their occurrence. A report on the value of urethrography to demonstrate urethral strictures after prostatectomy and observation on their etiology and prevention is now in print.⁷

Peri-urethral abscess Peri-urethral abscess is not a rare complication. It has been observed after all types of prostatectomy but most frequently after transurethral resection and especially in severe diabetics. Urethrography was invaluable for the recognition of this condition in those patients who complained of severe burning on urination and the diagnosis could not be made either clinically or cystoscopically. We have often been able to visualize the region where infection broke through the confines of the gland, the size of the abscess, and the direction toward which it points.

Urethral diverticulum We have observed four cases of urethral diverticulum found after the patient had a prostatectomy (fig. 4).

FISTULA EXTRAVASATION AND FALSE PASSAGE

Certain sequelae are the end results of surgical accidents which occur primarily during transurethral resection. Perforation through the prostatic capsule, the urethra, or bladder, and separation of the trigone are examples of complication.

- ⁵ Brodny, M. L. and Robins, S. A. Urethrography in bulbo urethral adenitis. *J. Urol.*, 43: 844-850, 1940.
- ⁶ Brodny, M. L. and Robins, S. A. The value of roentgenography of the male urethra following infection. *Am. J. Syphilis, Gonorrhea, and Venereal Dis.*, 32: 272-285, 1948.
- ⁷ Brodny, M. L. and Robins, S. A. Etiology of strictures after prostatic surgery. *J. Internat. Coll. Surg.*, 15: 459-471, 1951.

the chymotrypsin inhibitor value is greatly increased but the rennin inhibitor is found to be still higher, then the neoplasm is usually only slowly progressive, whereas the same chymotrypsin level in conjunction with a depression of the rennin inhibitor would be compatible with greater neoplastic activity. The attempt to control malignant disease thus involves the use of any therapeutic regimen which will depress the chymotrypsin inhibitor and elevate the rennin inhibitor. Maintenance of this status is the goal of palliative treatment.

Over 3500 patients have been investigated for all types of disease and over 50,000 determinations made during the past 3 years by Dr. Philip West. Technical requirements are minimal. Surprisingly, a centrifuge, pipettes, stop watch, water bath incubator, enzyme extracts and homogenized milk are the only laboratory equipment needed.⁶ However, the technician must be versed in the procedures of handling proteolytic enzymes or better still should serve as an under study in acquiring this technique for 3 or 4 weeks before reliable results are obtained.

This method is particularly applicable to control of adenocarcinoma of the prostate after the mucosa has regenerated following the removal of obstructing tissue. Approximately 20 determinations of the enzyme inhibitors may be made daily by one trained person. Preferably, he should be performing these in a laboratory providing sufficient material to occupy his undivided attention for accurate appraisals. This may pertain to larger laboratories or a pooling of interests.

Adenocarcinoma of the prostate which is limited to the confines of the capsule has not so far been found to induce an imbalance in the enzyme pattern. On the other hand, extension to surrounding lymphatics or to bone consistently produces considerable increase in chymotrypsin inhibitor associated with lowering of the rennin inhibitor in some instances. Successful palliation causes these abnormal serological findings to disappear. Reactivation of the neoplasm or recrudescence of osteoblastosis will again be disclosed by the imbalance in the enzyme pattern. This commonly occurs many weeks prior to the patient's complaining of discomfort or even months before there is any roentgenologic evidence of such activity.

Over 50 such patients have had numerous determinations of the enzyme pattern prior to operation or biopsy, after surgical intervention, after orchiectomy or after institution of hormonal therapy.

Case 3 LBVH No. 5678, C. S. The typical effect of orchiectomy is evident in the enzyme pattern of this 43-year old man (fig. 2, .1). There has been a remarkable shift in the enzyme pattern with rising rennin inhibitor and depression of the chymotrypsin inhibitor. Transurethral resection of prostatic carcinoma had been performed elsewhere in June 1948. Orchiectomy ameliorated discomfort due, presumably, to lymph nodes occluding the iliac artery. Biopsy of carcinomatous peri-aortic nodes was performed at time of sympathectomy. Small osteoblastic bone islands were detected in the iliac crest and femur.

⁶ West, P. M. and Hilliard, J. Proteolytic enzyme inhibitors of human carcinoma and disease. *Proc. Soc. Exper. Biol. & Med.*, 71: 169-172, 1949.

Routine postoperative urethrographic studies reveal a higher incidence of residual prostatic tissue than is generally realized. Fortunately, symptoms are not always present when tissue is left behind. The position of the overlooked lobes or commissures and their relation to the vesical neck, the external sphincter and the luminal continuity determines whether interference with urination continues.

The urethrogram is very valuable to demonstrate retained lobes and determine their size, location, and arrangement (fig 5). The voiding method of urethrography will often help clarify postoperative functional phenomenon. Follow-up urethrographic studies on patients with recurrent prostatism a few years after surgery have revealed enlargement of previously small residual adenoma-

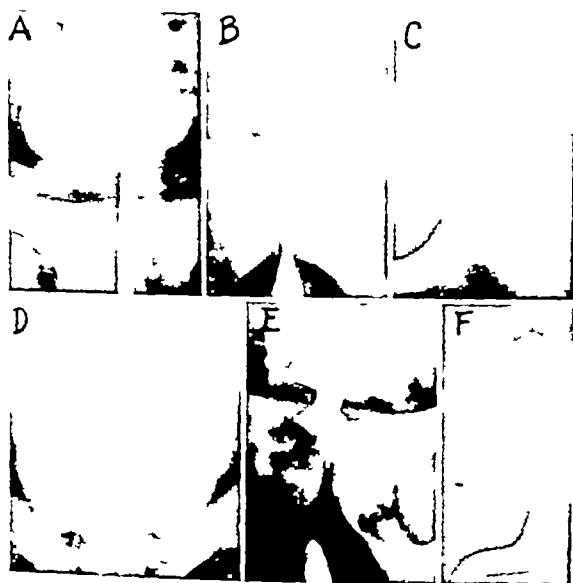


Fig 5 Retained prostatic tissue. A preoperative cystogram B preoperative urethrogram AP view C, preoperative urethrogram oblique view D postoperative cystogram E postoperative urethrogram AP view F, postoperative urethrogram oblique view. Note filling defect in outline of supracollicular urethra. This was due to suburethral adenoma which was not observed at time of suprapubic prostatectomy.

tous glands. Symptoms may develop when the patient is aged and secondary surgery is a hazard. Since the life expectancy of the man age 50-70 has almost doubled in the past 30 years, it is necessary for prostatic surgery to provide a satisfactory functioning urethral canal for a longer period. Incomplete enucleation of the prostate occurs during open surgery much more frequently than is generally realized. Entire lobes have been observed to have escaped the hands of even well-trained urologists. The incidence of residual prostatic tissue is lower with the one stage prostatectomy than with the two stage method due to the better opportunity to visualize the prostatic cavity. Incomplete removal of the adenomatous tissue is a common complication of transurethral resection. Tunneling of the prostatic gland leaves lobular stumps behind and gives a funnel-shaped appearance to the supracollicular urethra.

immediate improvement and androgen therapy may be continued safely for many months. Finally, however, the enzyme pattern reveals reactivation of the process at which time the hormone is discontinued and further remission ensues (fig 2, B). Variable response to testosterone is depicted by the enzyme pattern of two patients.

Case 4 LBVH No 3865, M L, aged 64, was admitted in May 1949. He had received stilbestrol daily since March, 1949. Fixation of the prostatic apex



FIG 3 Case 6

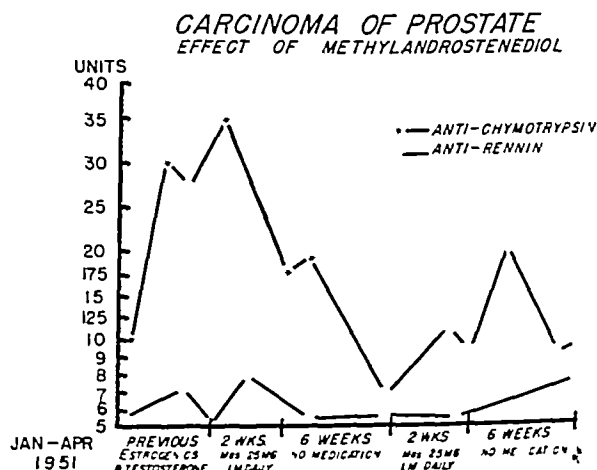


FIG 4

militated against perineal prostatectomy. Six months' relief was afforded by orchiectomy and prostatic resection. Estrogens alleviated his discomfort for a few months longer. Testosterone 25 mg was given intramuscularly each day for 1 week. This increased his pain and stimulated his carcinoma, as is evident from his increased chymotrypsin inhibitor. Repetitive therapy caused a similar response.

Case 5 LBVH No 14,530, J D, a 57-year old Negro, derived clinical benefit from testosterone without experiencing any disturbance in his well being. Decline in his chymotrypsin inhibitor is evident on this slide.

area 4) excrecent, superfluous scar tissues cause rigidity of the prostatic bed and restrict the action of the external sphincter 5) intrasphincteric, loss of urine may also occur after inadequate removal of prostatic tissue, especially when infected and when so situated as to interfere with sphincteric closure

We have observed calculi in the prostatic urethra after prostatectomy in three patients in whom dysuria, to the point of incontinence, and pain in the penis were prominent symptoms The etiology of these prostatic stones is speculative It was difficult to determine if they were vesical calculi which become lodged in the prostatic urethra or actually grew in a prostatic cavern

VESICAL NECK AND BLADDER

Hypertrophy of the interureteric ridge the trigone and the vesical neck which are not recognized and rectified at the time of surgery will produce postoperative symptoms These conditions should be classified as sequelae due to inadequate surgery The hypertrophied structures produce mechanical obstruction and are readily diagnosed by urethrography

Hypertrophy of the interureteric ridge appears on the anterior-posterior view as a V shaped filling defect above the vesical neck and in the oblique view as an anterior notching just above the trigone

Hypertrophy of the trigone produces a marked anterior angulation of the supracollicular urethra so that the internal orifice appears to deviate forward from its usual position and the base of the bladder is raised and tilts upward on the oblique view

Hypertrophy of the vesical neck is not infrequently overlooked at the time of surgery and will cause postoperative urinary dysfunction (fig 6) The high incidence of this complication has led some urologists to routinely include a wedge resection of the internal sphincter with their prostatectomy The postoperative retrograde urethrogram will show a triangular-shaped elongated collar constriction at the vesical neck On the voiding urethrogram, rigidity and incomplete opening of the vesical neck can be noted Adequate transurethral resection of these obstructions usually give good results Failure to remove sufficient tissue may lead to the eventual return of obstructive symptoms The vesical neck may fail to involute due to scar tissue, surgical excision, or neuromuscular dysfunction.

CONCLUSION

Urethrocytography supplements and complements instrumental examination in the appraisal of the end results of prostatic surgery

The local anatomical alterations produced by prostatectomy, the regrowth and healing of the supracollicular urethra in the uncomplicated case, and the structural deformities following complications can often be visualized

Urethrocytography is valuable to study the etiology of persistent symptoms after prostatectomy to record progress after treatment and to determine the need for further therapy

We wish to thank Miss Erica Carlan for the drawings in figure 1

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EPISPADIAS A REPORT OF FIFTEEN CASES

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Epispadias, known also as fissura urethrae superioris, in the male is characteristically a congenital defect in which the urethra opens on the dorsum of the penis. In the female the condition exists as a fission of the dorsal wall of the urethra and commonly extends to and involves the bladder outlet. Epispadias represents a lesser degree of the same embryologic developmental fault that produces vesical exstrophy and is always an anatomic component of exstrophy (figs. 1, 2, 3 and 4).

It is said that epispadias occurs about once in 30,000 individuals, and hypospadias is 150 times more common. Dees' statistical study of the incidence of epispadias suggests that it occurs, as deduced from hospital admission data (5,292,212) acquired by interrogation of several medical centers, about once in 117,604 males and once in 481,110 female admissions. It is notable that 15 or nearly a fourth of these recorded 56 hospital admitted cases of both sexes were at the Johns Hopkins Hospital where they were doubtless attracted by the skill and interest of Dr. Hugh Young who operated on 13 of them with reported good results in 12. Yet epispadias is probably not that rare. It was observed in three cases in 10,712 autopsies in boys studied by the writer, a ratio of 1:3570, as against 1:936 for bladder exstrophy. Fifteen personal cases have been seen, 12 of them in the office, and of this group which forms the basis of this communication, 13 have been operated upon. Epispadias associated with vesical exstrophy has been excluded from this study as has a most instructive sixteenth case in a 3-year-old boy seen in consultation with Dr. Edward Campbell of Philadelphia. More males than females have epispadias, the ratio in our 15 cases was 8:7. Being congenital, the condition has been observed at all ages, most of the reported cases being over 5 years of age, in our series two thirds were less than 5, and 3 were 8 years old (table 1).

This report is made largely to emphasize that when incontinence exists in epispadias, these patients should be surgically treated by plastic construction of a functioning bladder outlet and urethra rather than by ureterosigmoidostomy, the last method still being advised by some urologists and many general surgeons. By the plastic procedure not only can normal urination usually be established but the life expectancy of these unfortunate patients immeasurably extended over that so commonly observed to follow ureteroenteric transplantation.

ETIOLOGY

Among the many theories adduced to explain epispadias has been that of von Geldern (1924), the mechanical which assumes rupture of the bladder during fetal life and consequent to obstruction which has subsequently disappeared.

Read at annual meeting American Association of Genito-Urinary Surgeons, Sept. 2, Pa., May 18, 1951.

diagnostic effort is indicated. Postoperative cystoscopy when properly and gently executed is not a formidable procedure as preoperative cystoscopy often is when the highly sensitive mucous membrane of the posterior urethra is present and intact. Furthermore the economic aspect of cysto-urethrograms also must be considered as they are not without some cost.

Neither did we find visualization valuable in lesions of the distal urethra although it is admitted that sometimes one can see diverticula and small abscess-cavities. We are also not impressed with the value of this procedure in visualization of the membranous urethra or external sphincter region.

The greatest value from cysto-urethrography and especially the 'voiding' method is observation of the vesical orifice and bladder. The procedure may be useful in determining whether the internal vesical orifice is functioning and is an impediment to voiding. I recall two instances in which we carried out resection because of obscure and partial atony of the bladder. Postoperatively the 'holding' and voiding cysto-urethrograms showed that the vesical orifices still functioned and were competent when the patient made an effort to hold the urine. Subsequent resections removed all muscular action of the vesical orifice. In all prostatic surgery it is our confirmed opinion that best results follow the destruction or elimination of all muscular action at the internal vesical orifice. The latter should remain wide open at all times and the prostatic fossa is actually converted into a portion of the bladder. In this way all impediment to voiding is eliminated with the exception of the external sphincter and the usual resistance in the bulbous urethra. Visualization of the bladder by these procedures has often enabled us to recognize unsuspected diverticula and at times false passages under the trigone. The contour of the bladder may be indicative of detrusor disturbances.

It is therefore our conclusion that cysto-urethrography is more valuable for study of lesions of the bladder including neuromuscular function and of the vesical orifice. On fewer occasions it has been of value in lesions below the internal vesical orifice. It would seem to me that a sensible way to employ cysto-urethrography would be to not use it as a routine procedure but not fail to promptly utilize it as a diagnostic tool when the postoperative phase of prostatic surgery is accompanied by symptoms of prostatism, the causes of which are obscure after the use of the other diagnostic means in our hands. It is necessary for the observer to do enough of these procedures to become familiar with the technique and to be able to interpret a certain degree of physiologic function from the appearance of the plates.

Dr RUDOLPH BELL, Thomasville, Ga.: As has been shown, not every prostate gland is best suited for any one particular type of surgical approach.

I wish to emphasize two points. One is to advocate the routine administration of vitamin B in all retropublic prostatic cases. This may help to prevent the complication, osteitis pubis. The other is closing the prostatic capsule in retropublic prostatectomies. One encounters difficulty in placing the sutures in the corner of the incision opposite that in which the suture is started.

Dr ROY SUTSON, New York: I introduced the idea of starting a suture in

mesodermal structures comprising the abdominal wall from the genital papilla to the umbilicus

The hypothesis of Patten as reported by him at the 1950 meeting of the American College of Surgeons and based on embryological studies by him and his associates seems the most logical. Patten et al. rather reverse the usual explanatory sequence and believe the key to exstrophy lies in the embryology of epispadias. Granting that opportunities to study the embryologic development of epispadias in the human are wanting, they postulate a series of hypothetical stages in disturbed development which seem to explain the manner in which these associated anomalies may arise. They begin with the paired condition of the primordia of the genital tubercle which, as predisposing to epispadias and exstrophy formation, appear a little too far caudally with reference to the bladder outlet. This displacement would cause the primordia to lie at the level where the urorectal fold divides the original cloacal orifice into urogenital and

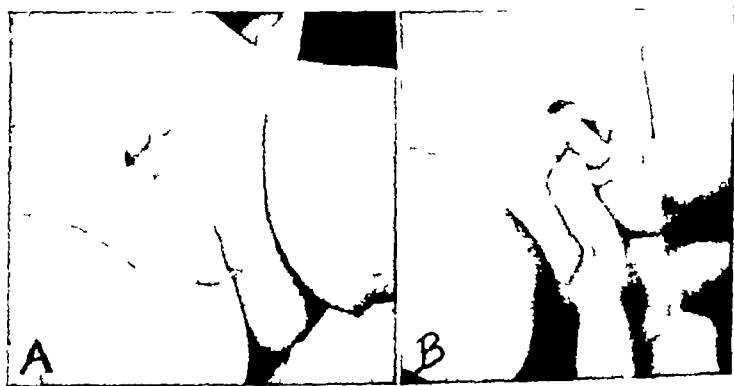


FIG. 3 Complete epispadias in a 14 month old boy. *A*, appearance showing stubby, staphylos penis with normal scrotum and descended testes. *B*, penis drawn forward showing divided corpora cavernosa and funnel-like extension of urethra beneath symphyseal band into bladder. Note pronounced ventral preputial redundancy.

anal outlets. Under such circumstances the corpora cavernosa would be formed just caudal to the urogenital outlet and the urethral groove would develop in their dorsal rather than in their ventral angle as is normally the case. Failure of midline conversion of the displaced paired primordia would account for the not uncommon exaggeration of the associated anomalies in which the penis or clitoris is represented by separate halves and molded about a single corpus cavernosum.

The exstrophy so generally accompanying the epispadiac condition involves a failure to reinforce the ventral body wall by convergent ingrowth of mesoderm. Normally this mesoderm ingrowth first occurs just cephalic to the urogenital orifice when the paired primordia of the genital tubercle meet each other in the midline. If these paired primordia are caudally displaced, this crucial spot remains over long without mesodermal reinforcement. Under these circumstances when the urogenital membrane ruptures, the opening into the presumptive bladder region will be much larger than normal and tend to extend in the midline.

THE AFTERMATH OF PROSTATECTOMY

ELMER HESS, RUSSELL B. ROTH AND ANTHONY F. KAMINSKY

From the Urological Department, St. Vincent's Hospital, Erie, Pa.

There are few subjects in the realm of Urology which are as dear to the heart of the urologist as that concerning benign obstructive enlargement of the prostate gland. If there is one staple item in the urological world, it is the enlarged prostate with all its accompanying inconveniences and disabilities. And, in spite of all the technical advances which are being made at a bewildering rate of speed on so many medical fronts, it appears that prostatism is destined to be with us yet for many years to come. We have gained no appreciable ground in efforts to avert the disease, we seem to be powerless to reverse the process by physical, chemical, or biological means, and we must content ourselves with the time-honored matter of surgical ablation of the obstruction. In consequence, there has been no shortage of attention to ways and means of accomplishing this latter end. At the risk of contradiction from certain partisan surgical technicians, we should ask you to grant, for the sake of argument, that present-day urological surgeons may tackle the obstructive prostate with equanimity by any of four fundamental routes, and since a recent paper was presented at the American Urological Association meeting in Chicago on infrapubic prostatectomy, it is not beyond the bounds of possibility that the number may shortly be increased to five.

It is not our concern here to go back over well-harrowed ground to argue which is the best method of prostatectomy. It is rather our purpose to bring up for consideration some of the criteria by which prostatectomy is judged. We are willing to assume that any urologist, certainly any young urologist with the necessary skill to do major surgery, may master the technique of any of the four or five procedures. We are willing to assume that, when performed by competent men, the various types of prostatectomy today carry approximately the same operative mortality. We are only too keenly aware of the fact that we may produce with ease a statistically startling series of cases by any one technique if we rigidly exclude from that series all our poor risks. In short, we are not currently interested in putting on trial any specific operative procedure. That, in our Clinic, has been done in the past to our own satisfaction, and with the conclusion that there are four good operations among which to choose in any given case. We are now tempted to concentrate our attention on what prostatectomy has to offer to the patient, on the reasonably justifiable assumption that he is going to survive the ordeal, however we may elect to carry it through. It is tempting to borrow the concept, so well worked out in the evaluation of treatment methods for cancer, of the five year cure. How will our patient be in five years? What, in this specific case, will the aftermath of prostatectomy be?

Our patient, in general, has little concern for how we go about the job of getting him well. He hopes, of course, to live through the procedure. But next in order, he hopes to be cured. He hopes to void freely, forcefully, and with pleasure.

Read at annual meeting, Western Section, American Urological Association, Sun Valley, Idaho, June 26, 1951.

TABLE 1

CASE	SEX	AGE	INCONTINENCE		LAPSPADIAS		PUPIB		GENITALIA		UPPER URIN TRACT		CYSTOGRAM PREOP	(CAPACITY) POSTOP	OPERATION	RESULT (CONTROL)	TIME TO ACQUIRE NORMAL CONTROL	ADDENDA
			Since birth	None	Complete	Incomplete	Separated	Normal	Excrcated	Divided clitoris	Kidney	Ureter						
1 J I	I	3 yr	+		+		+		+	+	Normal	Normal	Small	Normal	Young complete	Excellent	3 mo	Normal 20 years postoperative
2 C B	I	3 1/2 yr	+		+		+		+		Cong absence left	Absent left strict right	Small	Normal	Young sub pubic repair?	Excellent	18 mo	Absent left kidney and adrenal confirmed by exploration
3 I T	M	14 mo	+		+		+		+		Normal	Normal	Small	Normal	Young late closure of post-operative fistula	Excellent	1 yr	Died postoperative Normal now in college
4 I G	M	8 yr	+		+		+		+	+	Normal	Normal	Small	Normal	Young	Excellent		Behavior problem enuresis copresis
5 D D	I	3 yr	+		+		+		+	+	Normal	Normal	Small	Normal	Young	Fair	2 yr	Behavior problem enuresis copresis
6 C C	I	2 1/2 yr	+		+		+		+	+	Normal	Normal	Small	Normal	Young	Excellent	2 yr	Behavior problem enuresis copresis
7 C B	I	3 yr	+		+		+		+	+	Normal	Normal	Small	Normal	Young	Excellent	1 yr	Behavior problem enuresis copresis
8 J W	I	8 yr	+		+		+		+	+	Normal	Normal	Small	Normal	Young	Excellent	1 yr	Behavior problem enuresis copresis
9 D I	M	2 1/2 mo	+		+		+		+	+	Normal	Normal	Small	Normal	Young on bladder neck and distal urethra	Excellent	2 yr	Normal night and partial day control steadily improving
10 C B	M	2 yr		+		1 to 1 1/2 tub		+			Normal	Normal	Small	Normal	Young on bladder neck and distal urethra	Fair		Normal night and partial day control steadily improving

up against the same unanswered question: What are the advantages offered by the various techniques? In the long run, this can only be answered by close attention to late results. And when the late results of prostatectomy are good, our patient with the 5 year cure, it must be assumed that for that patient a proper choice of approach was made. If we have done nothing but resections, we are in poor position to evaluate the other operations. The partisan operator, in other words, is in a fine position to advance and refine his own particular technique. His contribution is a major one in clinical and technical research, and we should encourage him. But we should be cautious in listening to him when he departs from his accustomed sphere and starts making comparisons to techniques of which he is not the master. Our question is most likely to be answered by analysis of late results in an experience which has encompassed all approaches to the prostate.

From our Clinic, we feel some justification in setting forth our impressions. The senior author was for a long period of time what might be called an 100 per cent resectionist. Certainly, every case was resected wherein there was not a distinct and unquestionable contraindication to it. Another of us was trained by the late Hugh H. Young. It is scarcely necessary to mention by what approach he preferred to accost a prostate. To this we have added a series of some 300 cases done by the retropubic route, and our files assure us that we have a sufficient number of cases done by time-honored suprapubic transvesical method to give us some right to claim familiarity with it. A great many considerations, however, restrain us from a statistical analysis. A valid statistical analysis of 5 year results may be projected for the future when we have been attempting to fit the procedure to the case for a longer period of time. At present, we can only record impressions, and we should not wish to invest these impressions with the misleading cloak of mathematical certainty which statistics so often imply. Suffice it to say that in our Clinic we are now seeing patients, operated on 5 or more years ago, wherein we may exercise hindsight and conclude that the patient would have been better off if we had done otherwise than we originally did. This means that we are seeing long continuing or late recurrent morbidity assignable to the prostate gland, and for purposes of discussion, we may break these cases down into broad categories.

First, there is the recurrent or persistent prostatic obstruction. When this is encountered, we must attempt a differentiation between inadequate initial removal of obstructive tissue, and a recurrent formation of adenomas. Here, we encounter the late result which has been the greatest single factor in dampening our enthusiasm for resection. The overwhelming majority of our problems on this score arise in patients who were resected. We fully admit that it is an occasional problem with the open routes, but we have been forced to the conclusion that when we decide upon transurethral resection as the operation of choice, it must be with the full recognition of the distinct possibility that if the patient lives for more than a few years, he will require additional prostatic surgery, or will be subject to recurrent obstructive morbidity. It is the factor that is leading us to conclude more and more that the younger men, and all men in sound physical condition aside from prostatism, should have open enucleations rather than

In the female epispadias is generally of the complete variety, other types of lesser severity are designated as clitoric and subsymphysal. The degree of bifid clitoris and prepuce and the wide separation of the labia and pubic bones reflect the severity of the malformation (fig 4). The vagina and pelvic organs are usually normal. Yet in case 2 the imperforate hymen was a dense wall of fibrous tissue and the cervix was lobulated, and in case 7 the labia minora were notably absent as they so frequently are in epispadias in this sex.

As in all types of genital anomalies, the upper urinary tract is maldeveloped in about one in three cases. In case 2, there was left hemi-atrophy of the trigone

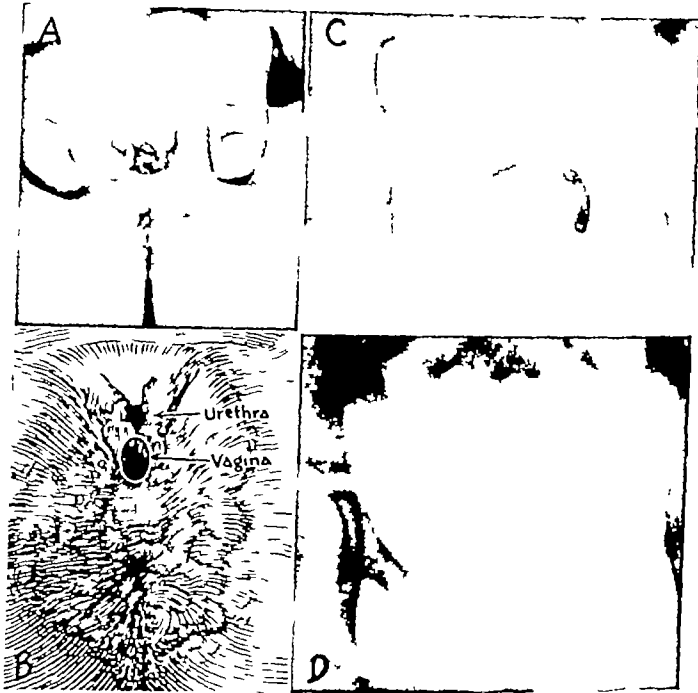


FIG 4 Complete epispadias. *A*, in a 3 year old girl. Cleft clitoris with pronounced vulvar and peri-anal excoriation consequent to continuous urinary leakage. *B*, schematic of conditions present. *C* and *D*, complete epispadias. Cystography in patient shown in *A* and *B*. *C*, note absence of symphysis. Catheter is coiled in bladder which would retain no cystographic medium. *D*, postoperative cystogram, essentially normal capacity, normal urinary control.

with congenital absence of the ureter and kidney above, while in a sixteenth case not included here, nephrectomy for congenital infected right hydronephrosis had been performed at 6 weeks of age.

There is often incontinence which unfortunately sometimes causes the child to be treated for enuresis, excoriation of the skin by the continuous wetness may be extremely painful and the child is usually marked for social ostracism (fig 4, *A* and *B*). Urinary incontinence and its sequels together with the malformation itself are the clinical manifestations and as these children with epispadias grow older, they or their associates note the abnormality which, though asymptomatic, may produce a marked genital fixation complex (cf. Novak, 1918). In rare instances there may be stenosis of the external meatus of the epispadiac canal.

that he who does many perineal operations will end up in the rectum more than once, and he who goes transvesically will perhaps open the peritoneum or cause a most terrifying hemorrhage. He who is learning the retropubic approach will likewise not escape unscathed. These facts are not indications or contraindications for any technique. It would be purely a personal expression of opinion to say that it is hardest to become a good resectionist, next most difficult to master the perineum, and easiest to do a creditable suprapubic transvesical enucleation, but it is only fair to repeat a personal conviction that, under present-day circumstances of urological training, and with present-day instruments and surgical adjuncts, it is completely possible for any young doctor with average aptitude to become proficient in all methods.

In summary, we might say that it has become our habit to pay serious attention to the aftermath of prostatectomy, and to ask ourselves in each case of continuing or recurrent urological morbidity after prosthetic surgery, 'How might we have avoided this difficulty?' Since we are no longer devotees of one special school of surgical technique, we feel no compunctions in concluding that we might have done better by using an alternative approach.

Such analysis of late morbidity has led us to abate our enthusiasm for endoscopic resection, and to increase our respect for clean open enucleation, preferably under direct vision. The fact that we have multitudes of '5-year cures' after resection proves to our minds that it is an operation of great virtue and one which we must continue to utilize in a significant percentage of selected cases. Our impressions do not constitute a condemnation of any one of the four standard techniques. We do not conclude that the analysis of our late results indicates how anyone else should approach a prostate, but we do feel that from it we are gaining valuable information as to how we, ourselves, should proceed in any given case.

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epispadias, perineal urethrostomy drainage is satisfactory as long as perfect tube function can be maintained. In two of our cases the perineal tube (16F balloon catheter) ceased to operate properly because of phosphatic and mucus deposit,

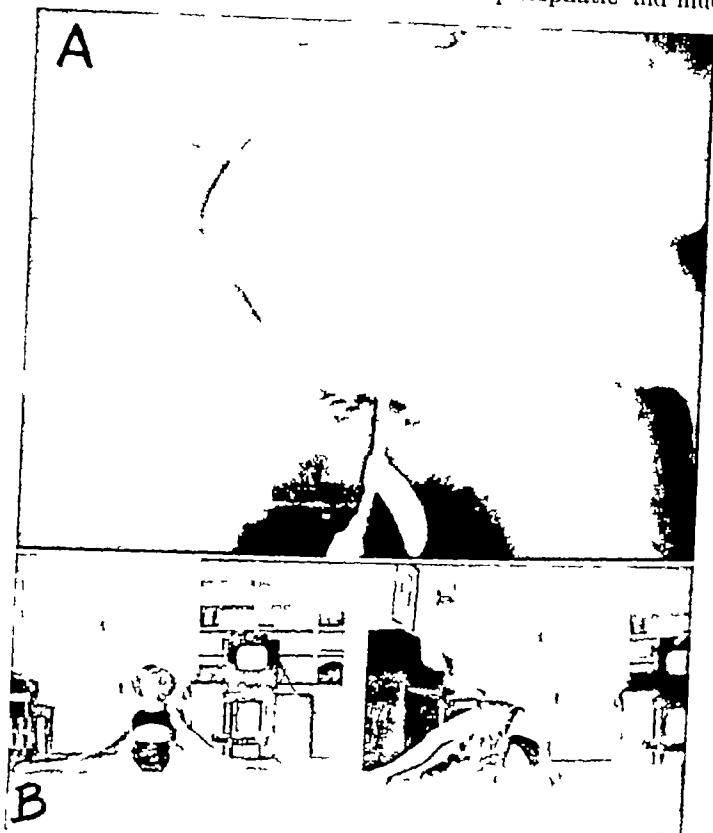


FIG 5 Complete epispadias in a 3 year old girl. A, postoperative cystogram showing relatively normal bladder outline with normal capacity, absence of symphysis and silver wire with which symphyseal pubic band was sutured together. Normal control B, 2 years postoperative, patient engaged in aerobic dancing, no orthopedic difficulties nor physical handicap.



FIG 6 Complete epispadias in an 8 year old boy. A, dorsal penile fistula development, postoperative, and requiring secondary closure with perineal urethrostomy counterdrainage. B, late result following closure of fistula in B. (Sound in urethra.)

some urine passed forward in the urethra to meet local wound breakdown in one instance but which spontaneously closed with the reestablishment of proper drainage.

Plastic construction of a penile urethra can be performed by any of several

infection as well as neoplasms produce an increase in the chymotrypsin unitage⁴ In fact, any condition which induces a negative nitrogen balance is associated with a reversal of the normal equilibrium between chymotrypsin and rennin inhibitors The tentative assumption is that, in some manner, chymotrypsin inhibitor reflects the rate of protein degradation while rennin inhibitor seems to be allied with protein synthesis, and that the enzyme inhibitor pattern expresses the balance that exists between these two phases of protein metabolism

The most rapidly growing tumors occasion maximum dissociation or reversal of the equilibrium between the two inhibitors (fig 1) This is manifested by high chymotrypsin inhibitor and low rennin inhibitor values Arrest or regression of the neoplasm is found to be associated with values of 15 or better for rennin inhibitor and less than 5 for the chymotrypsin inhibitor⁵

Case 1 LBVH No 1038, P B, a 58-year old man, obtained 4 months' relief after orchiectomy and transurethral resection for prostatic carcinoma with

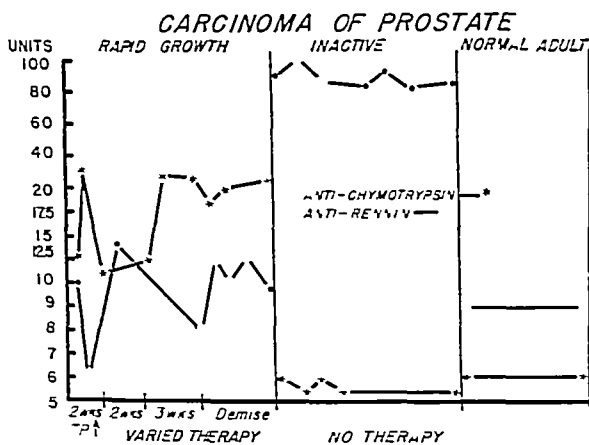


Fig 1 Graph in left portion of illustration is that of case 1, graph in midportion is that of case 2

skeletal metastases His course is representative of patients whose enzyme pattern is unresponsive to therapy The rising chymotrypsin inhibitor and falling rennin inhibitor are evident on the left hand portion of this figure In fact, he was resistant to estrogenic, androgenic and roentgen therapy

Case 2 LBVH No 14,733, D H, age 65 The patient's enzyme pattern depicts excellent control data He was first seen in July 1949, at which time perineal prostatic biopsy confirmed the suspicion of adenocarcinoma Orchiectomy was refused and he has received no therapy for the intervening period of two years The enzyme pattern discloses a remarkably high rennin inhibitor value, even though no hormone therapy has been administered

Calculation of the patient's response to any particular therapeutic modality is dependent not on the chymotrypsin inhibitor or rennin inhibitor alone but on the balance maintained by the enzyme pattern For example, in the event

⁴ West P M, Rappaport, S I and Tempereau C E Enzymatic evaluation of therapeutic agents in cancer Cancer, 4 177-183, 1951

⁵ Ellis F and West P M J Clin Invest In press 1951

adjacent urethra, the shiny hairless mucosa-like skin being mobilized from the subpubic and prepubic areas in pouch formation and reflected forward. Dorsal penile skin mobilized as longitudinal lateral flaps, which were brought together in tube formation, completed the urethral construction proper. After constructing the new penile tube, the penis with its dorsal raw area was implanted in a

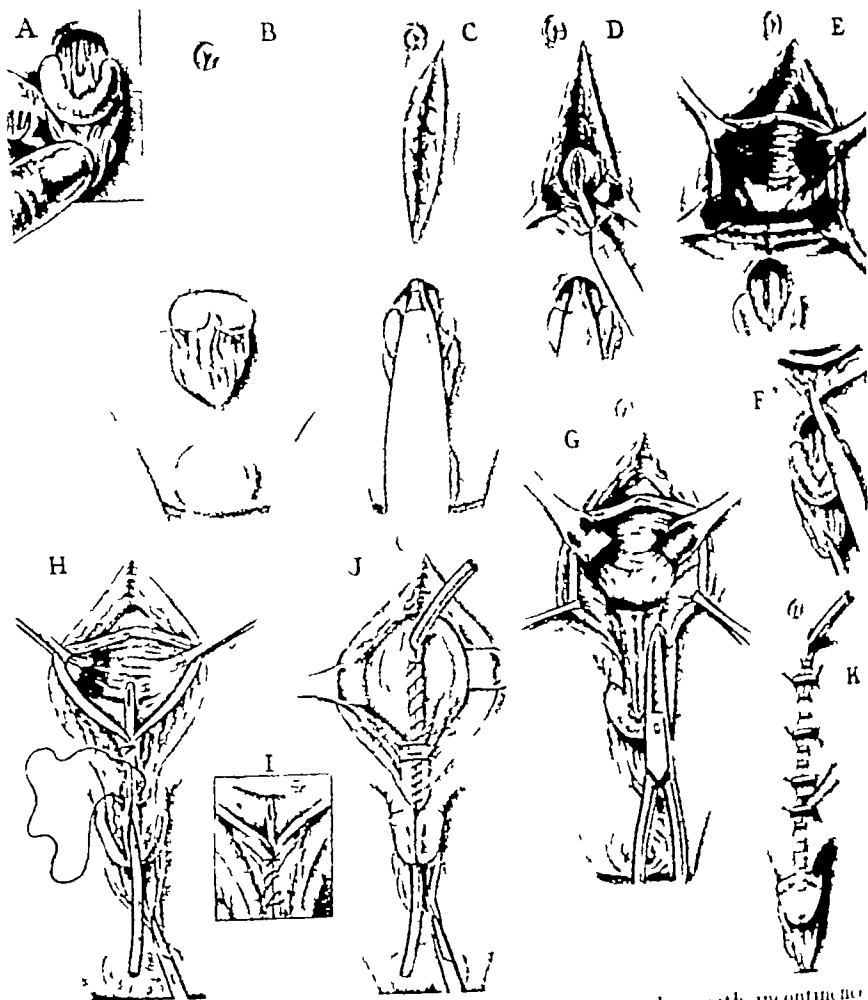


FIG. 8. Young's operation for correction of complete epispadias with incontinence in male. Various steps being essentially those given in legend of figure 7 but here, in addition, showing plastic correction of epispadias. (Redrawn after Young.)

tunnel made beneath the skin of the anterior scrotum and, when healing occurred, the penis was liberated much as in the Cantwell operation for hypospadias.

Having performed the operation to establish urinary continence in epispadias, the surgeon should not feel that he has failed if the patient leaks immediately postoperative. In two of the writer's cases the achievement of perfect control took as long as 2 years (table 1). Here grave behavior problems retarded normal bladder control despite a technically satisfactory operation, in one girl the in-

The effect of estrogens has been studied only after orchiectomy and the findings are therefore less dramatic, but the need for increased dosage is plainly indicated when the chymotrypsin inhibitor value rises. Estinyl 0.5 mg tablets orally have been utilized in the main. After estrogen resistance has occurred, cessation of therapy is rewarded by a decline in the chymotrypsin inhibitor value in many instances.

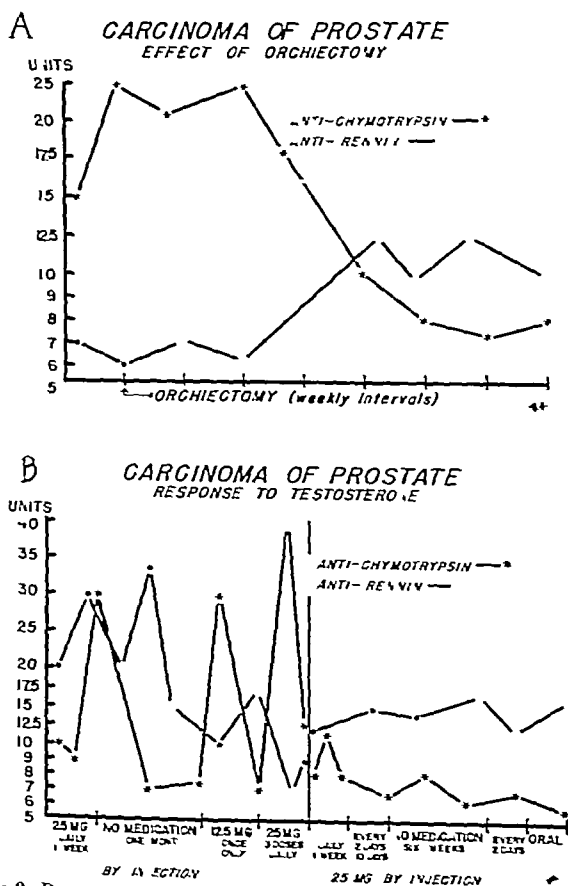


FIG 2 4, case 3 ^{BY INJECTION} graph in left portion or illustration is that of case 4, graph in right portion is that of case 5 ^{25 MG BY INJECTION}

Rather surprising effects have been gained by instituting testosterone therapy in those patients who no longer responded to anti-hormone therapy. Two contrasting types of response have been observed and therefore caution is urged in its usage. One group is characterized by extreme testosterone sensitivity and administration of only 12.5 mg, may produce profound rise in the chymotrypsin inhibitor level concomitant with marked deterioration of the patient. Death has occurred within 24 hours after a single 50 mg injection. Strangely, if the patient survives, recession may occur following this startling clinical and enzymatic evidence of exacerbation. The second group (about 75 per cent) derives

Case 6 LBVH No 12,437, R L Roentgenogram of the bony pelvis revealed the profound bony metastases which had been present from the time this 54-year old patient was first seen in January 1949 (fig 3) Prostatic resection and orchiectomy were performed in August 1949 The markedly dense osteoblastic production affected all bones excepting the arms and hand Little alteration was effected by castration or by estrogenic therapy but there has been complete arrest of the neoplastic process as determined by serial enzyme patterns and skeletal x-rays Since institution of testosterone therapy he remains completely asymptomatic and has gained thirty pounds The present dosage of testosterone propionate is 25 mg , intramuscularly, each week

A newer male sex hormone devoid of virilizing effects, methylandrostenediol exerts protein anabolic action in constitutional diseases accompanied by protein wastage (fig 4)

The enzyme pattern of this patient was utilized in the slide depicting one who suffered constitutional symptoms and rather marked rise in chymotrypsin inhibitor with testosterone administration Methylandrostenediol was well tolerated in doses of 25 mg daily, intramuscularly, for 2 weeks before evidence of toxicity occurred Following this milder hormone treatment there was a similar remission and improved enzyme pattern as had been achieved with testosterone but without the alarming side effects The same therapy was repeated in March, resulting in a second period of improvement

SUMMARY AND CONCLUSIONS

Serial determination of chymotrypsin and rennin inhibitors of the serum provide a sensitive method for gauging the therapeutic control of neoplasms

Actively growing adenocarcinoma of the prostate with extension or skeletal metastases causes a disturbance in the normal balance between these proteolytic enzyme inhibitors

The degree of control obtained in prostatic carcinoma following orchiectomy or estrogen therapy may be measured objectively by observing the resulting changes in the concentration of the two factors

The sensitivity of the method permits ready evaluation of other steroids such as testosterone, progesterone and methylandrostenediol in patients who have become estrogen resistant

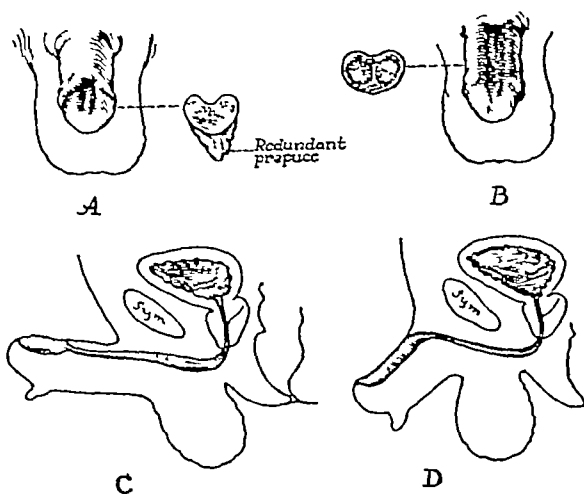


FIG 1 Varieties of epispadias A, glandular, rarest variety Prepuce appears as a ventral hood A', lateral view showing slight dorsal chordee, urethra is continuous through superior segment of penis and terminates as a groove in glans (C) B, penile, meatus opens at base of the organ, corpora cavernosa being partially divided Note absence of corpus spongiosum D, schema of condition in B, proximal urethra is normal

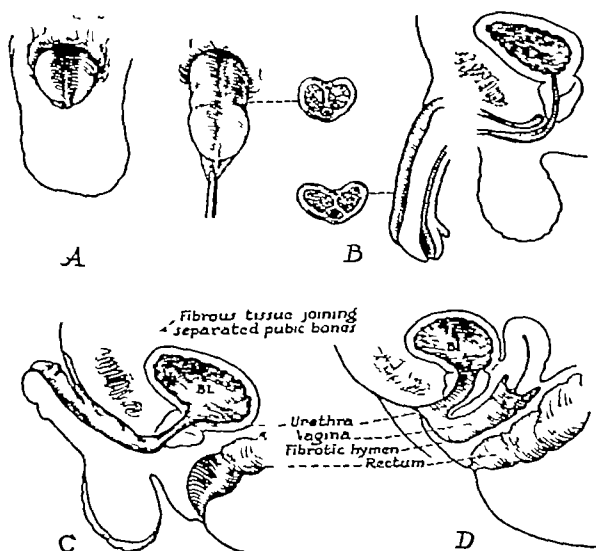


FIG 2 A, subsymphiseal epispadias B, subsymphiseal epispadias in case 2, table 1, canal being essentially a reduplicated or accessory urethra ending blindly in a slight bulbous dilatation at triangular ligament Excision C complete epispadias in male representing a first degree exstrophy D, complete epispadias in a 13 month old girl (case 2) in which bladder was widely opened to outside there being no true urethra Vagina was obstructed by an extremely dense fibrotic imperforate hymen and cervix was lobulated but could not be proved to be reduplicated Congenital solitary right kidney coexisted

Keith's theory (1908) assumes the occurrence of intra-uterine ulceration of the anterior bladder wall of the fetus Mall (1908) and Wyburn (1937) attribute the anomaly to failure of mesoderm to develop locally and Gillies hypothecates a forward displacement of the cloacal membrane with failure to develop of the

to the umbilicus. The likelihood of such an extension is enhanced by the exceedingly rapid elongation of the region between the urogenital orifice and the umbilical cord which occurs at this stage of development. Even slight retardation of mesodermal ingrowth under such circumstances would in all probability mean a delay in reinforcing the region sufficient to account for the characteristic extensiveness of the exstrophic defect. Thus is explained not only the genesis of the minor epispadiac developments but also those involving lack of development of the urethra and the bladder outlet—the type so commonly seen in the female as it was in the seven young girls in our series.

CLINICAL MANIFESTATIONS

All gradations of epispadias occur, the incidence of the condition being in direct ratio to its gravity (fig. 1). Of the incomplete varieties in the male, the simplest yet the rarest is the glandular or balanitic in which the urethral opening is above and behind the glans (fig. 2). The dorsal groove indents the glans forward to its tip and causes this portion to be flattened out.

In penile epispadias the urethral opening may be at any point from the postglandular sulcus to the suspensory ligament and is generally near the base of the penis (fig. 1, *B*). The dorsum of the penis is therefore grooved from the epispadiac meatus to the tip of the glans or may terminate proximally. In one of our cases (No. 12), the epispadiac canal was that of a reduplicated or accessory urethra extending back to the triangular ligament (fig. 1, *C*). The sulcus in epispadias is covered by urethral mucosa and is frequently dotted with the orifices of the ducts of the peri-urethral glands. The prepuce hangs ventrally as a loose tag (the reverse of hypospadias) and leaves the broad flattened glans uncovered (fig. 3). The corpora cavernosa are usually widely separated and the corpus spongiosum is hypoplastic or may even be absent. As a rule the organ is smaller than normal, is spatulous in appearance, and incurved upward. Prostatic development is poor, is often incomplete above or is here entirely lacking. Because of these defects and even though erection occurs, intercourse is difficult or impossible and in the more severe forms of epispadias insemination will not occur.

In penopubic or subsymphyseal epispadias the urethral defect extends beneath the pubis to or nearly to the triangular ligament, when the defect does not involve the triangular ligament and the external sphincter muscle, urinary control is generally normal as it was in five of our cases in the male.

In complete epispadias in the male, the urethra is open to the bladder neck as a broad deep funnel and the condition is often associated with early degrees of vesical exstrophy (figs. 1, 3 and 4). In 6 such cases (females) in our series, the finger could be inserted into the open bladder outlet. The pubic bones are usually ununited and sometimes are rudimentary (fig. 4, *B*, *C* and *D*). Yet the separated bones are joined by a dense fibrous transpubic band. For these reasons complete epispadias may be considered a first degree of exstrophy, and with negligible or no sphincter development total incontinence is the rule. In case 3 the verumontanum was unusually large and in case 10 there was bilateral cryptorchism with a congenital hydrocele of the cord and hernia on the left side.

DIAGNOSIS

This is made by inspection in which the anatomic conditions previously described will be observed. Often the finger can be introduced through the epispadiac canal directly into the bladder. Excretory urographic study is advised in these cases as there is approximately a one-in-three chance that the upper urinary tract is also anomalous, moreover, other unsuspected disease of vital importance may be disclosed.

TREATMENT

This is surgical and properly executed according to indication may be expected to restore the penile urethra to a normally functioning canal which discharges at the usual site or, when the patient is incontinent, to construct a vesical outlet which, aided by subsequent surgical stricturization, will instate normal bladder function and schedule of urination.

In the construction of a new vesical outlet, the operation should be postponed until the child is at least thirty months of age—in short, until the age at which vesical control is normally achieved. Even after this age, the patient is certain to have some difficulty in learning to void and control his bladder, for it is a new and important experience which has previously been denied.

Young's operation with modification has given the best results in our hands in the correction of the incontinence in epispadias (figs. 7 and 8). In 8 of the 9 cases in which we have employed this procedure (5 females, 3 males), the incision has been through the midline dividing the pubes and widely exposing the vesical outlet and entire urethra. In case 2, a $3\frac{1}{2}$ -year-old girl, the procedure was carried out from below and with a most satisfactory result. As shown in figure 7, the urethral mucosa at the vesical outlet and in the adjacent urethral segment is largely cut away, leaving only a narrow strip, usually not over 3 to 5 mm wide, but attempting to leave as much as possible of the musculature at and adjacent to the vesical outlet. This large muscle mass is then sewn together with No. 0 chromic gut, closing over both the urethral strip of mucosa remaining on the urethral floor and a fine (30) stainless steel suture wire which passes from above through the open bladder, the bladder neck, the urethra, and out the meatus for future use as a guide for a tunneled sound should this become necessary for urethral dilation three weeks or so postoperative. Fortunately we have had to use this guide in this manner in only one case (No. 6). Young reported a dense postoperative fibrotic occlusion of the bladder neck following the operation in one of his cases.

Following division of the pubis for direct access to the bladder outlet, and its closure with silver or stainless steel wire, no cosmetic or orthopedic difficulties have been observed in the children reported here (figs. 4, 4 and B, 5, and 6). That this procedure is unlikely to cause physical disturbances or handicap is suggested by case 7, a girl now seven years old who, two and a half years postoperative, engages without discomfort in semiprofessional acrobatic dancing (fig. 5).

When the operation is performed with splitting of the pubes, urinary counter-drainage is established by cystostomy tube (fig. 8). In the correction of penile

methods, the writer has employed that advocated by Young (fig 8) in 3 cases, the Thiersch technique in 1 case, and has used the Denis Browne pro-

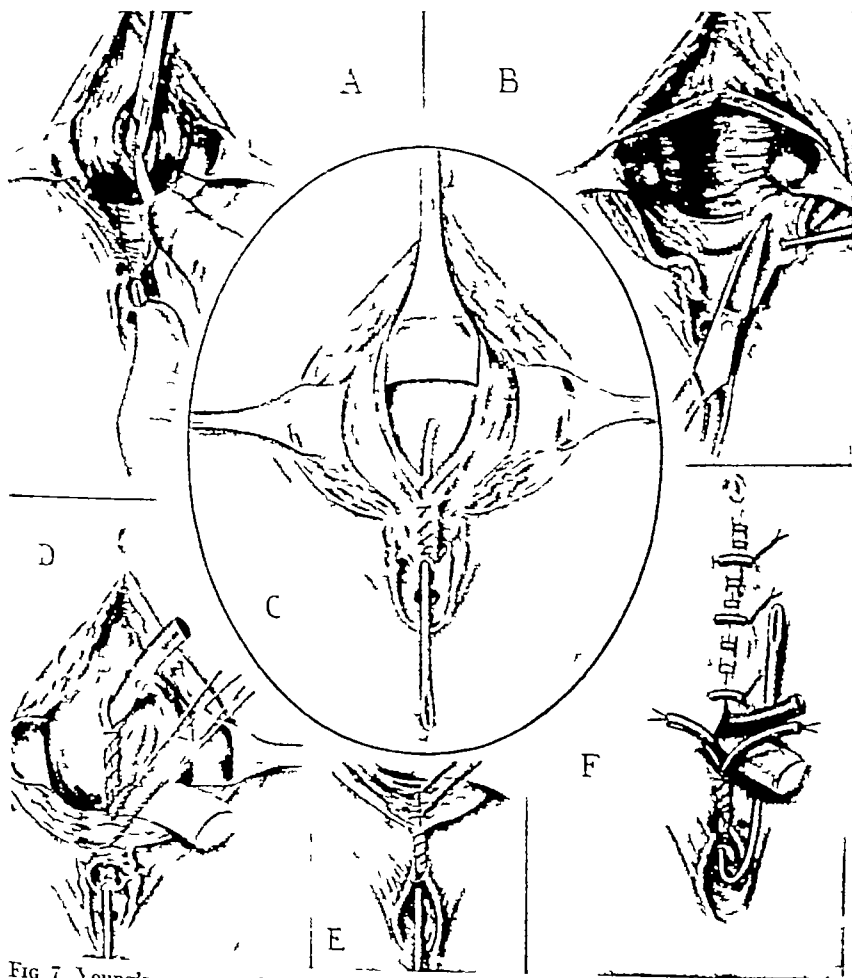


FIG 7 Young's operation for complete epispadias in female 1, laying open of bladder outlet and entire urethra by division of pubis *B*, excision of mucosal redundancy at bladder outlet, our practice is to excise mucosa considerably more widely than Young indicated but to leave a mass of muscle tissue as large as possible about the bladder outlet *C* closure of bladder outlet and construction of urethra about a small silver probe as recommended by Young. Author prefers to use a steel wire for this in order to get closure of maximal tightness and to leave wire in situ as a guide for passage of a tunneled sound 2 to 3 weeks post-operative should this become necessary as occurred in one of our cases *D* closure of bladder about a suprapubic drainage tube *A* cigaret drain is left in the space of Retzius for 48 to 96 hours Approximation of interpubic fibrous band using silver or steel wire *E*, *F*, external closure (Redrawn after Young)

cedure in 2 cases The Browne procedure is carried out substantially as it is employed in the correction of hypospadias

In 2 cases without incontinence (Nos 11, 12) a modification of the Ombrédanne operation for hypospadias was employed to construct the subpubic and